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ORIGINAL ARTICLES.

SHORT-DURATION TYPHOID FEVER.[1]

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The term short-duration typhoid fever is used to include the types of the disease which have been designated ambulatory, abortive, mild, typhus lævis, and typhus lævissimus. These types are not well defined, and it seems desirable to have a term which not only will include them all, but at the same time will point out the very important fact that many cases of typhoid fever do not run the classical twenty-one day course. The mild and ambulatory cases come within the meaning of the term only when they last less than three weeks.

Every year during the typhoid season a limited number of patients enter the second medical division of Bellevue Hospital suffering from a mild febrile disease, without obvious cause, which completes its course in periods varying from about one to about two weeks. During the first years of my service at the hospital, in accordance with accepted beliefs, I regarded these cases as examples of febricula or simple continued fever. In 1901, however, when I undertook with Buxton to study the bacteriology of the blood in typhoid fever, I began to question the correctness of this diagnosis. About this time the paratyphoid infections attracted the attention of numerous investigators in Europe and in this country, and the claim was made by several writers that the paratyphoid could be distinguished

[1] Read at a meeting of the New York State Medical Society, Albany, January 26, 1909.

clinically from the typhoid cases by their milder and shorter course. With the double purpose of testing this claim and of determining the true nature of the disease or diseases in question, we made bacteriological examinations of the blood of all patients who might be suffering from typhoid fever. The recovery of the typhoid bacillus in pure culture from the blood of several of these cases convinced me that the whole question of the occurrence and diagnosis of the irregular forms of typhoid fever might be profitably investigated.

REVIEW OF THE LITERATURE. Though typhoid fever has been known as a distinct disease for nearly a century, a review of the literature reveals an astonishing state of confusion concerning the very existence of the milder and shorter forms. The history of the diagnosis of typhoid fever falls readily into two periods: (1) The period before the introduction of exact methods of diagnosis; and (2) the period since the application of the Gruber reaction by Widal to the diagnosis of typhoid fever and the general employment of bacteriological methods in the diagnosis of the disease.

First Period. While the diagnosis of a typical case of typhoid fever ordinarily presents no difficulty, supposedly typical cases have occasionally turned out to be acute general tuberculosis. There is no clinical means by which the diagnosis of typhoid fever can be positively established. Therefore the diagnosis of the disease in this period was necessarily a matter of opinion. In a disputed case the diagnosis could not be proved or disproved unless some typical or fatal complication developed and the case came to autopsy. Ordinarily the "weight of authority" prevailed in doubtful cases.

The fact that mild forms of typhoid fever did occur, however, was known very early in the history of the disease. Louis[2] saw a case of ambulatory typhoid which perforated and came to autopsy. These forms were described by Wegelin[3] in 1854, by Griesinger[4] in 1864, by Murchison[5] in 1873, and by Liebermeister[6] in 1874. In 1873 Jurgensen[7] said that the whole theory of infective diseases is untenable if the existence of milder forms cannot be shown; that transitions from the mildest to the severest must be demonstrated.

Yet during the same period there grew up an extensive literature on mild fevers which were not generally, at least, considered to be typhoid and upon which a variety of names were bestowed. Some of these names may be cited: febricula, simple continued fever, mountain fever, "New York fever," embarrass gastrique febrile, fièvre bilieuse simple ou inflammatoire, gastrisches Fieber, and febris gastrica. Fortunately, these names have given place largely to

[2] Recherches sur la maladie fièvre typhoide, Paris, 1841.
[3] Zurich Thesis, 1854 (quoted from Briggs; original not available).
[4] Infktskrankh., 1864.
[5] A treatise on the continued fevers of Great Britian; London, 1873.
[6] Ziemssen, Path. u. Ther., 1874, vol. ii, Acute Infktskrankh.
[7] Volkmann's Samml. klin. Vortr, 1870, i to xxxiv; Inn. Med., No. 21, p. 477.

more exact diagnoses. But for many years it was claimed by English army surgeons that there was no typhoid fever in India. As late as 1897, the late Sir Joseph Fayrer[8] stated that "enteric fever occurs in India as it does in Europe, and most probably has always existed there. It may have been confounded with continued or remittent malarial fever, but it is not by any means certain that a febrile condition accompanied by diarrhœa, Peyerian ulceration, and an abdominal eruption is necessarily caused by the one specific contagium to which it is attributed in Europe." (At the time this was written the paratyphoid infections had not been studied). In the same article the fever morbidity returns for 1892 of the European and native armies in India, numbering nearly 200,000 men, are given: they were 1563 cases of typhoid fever, 96,226 cases of intermittent, 2660 of remittent, and 5618 *cases of simple continued fever.*

Likewise, for many years it was denied by the French army surgeons that typhoid fever existed in Algeria, but Scherb[9] states that typhoid is more common in Algeria than in Paris. Denis[10] says that typhoid fever in the corps in Algeria is almost as great as in the whole army in France.

It is true that the existence of these fevers as distinct diseases was called into question from time to time. Bäumler[11] said in 1867 that the earlier German idea that there existed a "febrile gastric catarrh" as a distinct and not uncommon disease, which in fully developed form was considered "gastric fever," had been gradually abandoned in favor of the belief that it was typhoid fever. Levy[12] in 1886, and Chantemesse[13] and Courtet[14] in 1889, expressed the opinion that embarrass gastrique febrile was a mild form of typhoid fever.

Undoubtedly one reason for the reluctance of the medical profession to accept, during this period, the belief that the milder forms of typhoid fever occurred frequently was the weight of Wunderlich's[15] dictum, issued in 1868, to the effect that a case of fever, without obvious cause, was certainly not typhoid unless the temperature reached 103.2° between the fourth and sixth days. In the absence of exact methods of diagnosis, one might doubt but not disprove the truth of this dictum. As late as 1897, Dreschfeld[16] referred to it as still possessing value in diagnosis.

Second Period. The second period opens with the announcement by Widal[17] of his application of the Gruber reaction to the diagnosis of typhoid fever. Strange as it may seem, when one considers the

[8] Allbutt's System, article on the Climate and Some of the Fevers of India, vol. iii.
[9] Bull. méd. d'Algerie, 1903, 2s, I, 33.
[10] Discussion of Scherb's paper.
[11] Deut. Arch. f. klin. Med., 1867, iii, 278.
[12] Thèse Montpellier, 1886, Embarrass gastrique febrile.
[13] Sem. méd., 1889, ix, 421.
[14] Thèse de Paris, 1889, Embarrass gastrique febrile et typhoide fièvre.
[15] Das Verhalten der Eigenwarme in Krankheiten, Leipsic, 1868.
[16] Allbutt and Rolleston's System, article Typhoid Fever.
[17] Soc. méd. d. hôp. d. Paris, 1896, 3s, xiii, 561.

epidemiological importance of the subject, the study of the milder forms of typhoid fever, with the aid of exact methods of diagnosis, has been greatly neglected.

Shortly after the appearance of Widal's paper it was demonstrated in France and Tunis by Lemoine,[18] Catrin,[19] Geraud and Remlinger,[20] and Roux[21] that serum from cases of embarrass gastrique febrile gave the typhoid reaction. Woodruff[22] showed that this was also true for mountain fever in this country. (It may be stated parenthetically that these results would not be accepted today because the methods of performing the tests have since been shown to be unreliable. Yet these investigations marked a definite advance in the study of typhoid fever.)

In 1904, during the typhoid epidemic in and around Saarbrück, Koch and his co-workers established the typhoid nature of many mild febrile cases of indefinite clinical character. For example, Drigalski[23] obtained a positive typhoid reaction 306 times and recovered the typhoid bacillus from the stools 75 times in 381 doubtful cases. Frosch,[24] by the employment of the same methods, discovered 144 cases of typhoid fever in a region where only 8 had been officially reported.

J. P. Bates has published the results of a study of 68 cases of typhoid fever in Panama.[25] Twenty-one (32 per cent.) of the cases were of the short-duration variety. The typhoid bacillus or a paracolon bacillus was recovered from the blood in 9 of these cases; in the 12 remaining cases the diagnosis was based upon the serum reaction. A paracolon bacillus was found in the blood of the case of shortest duration (eight days).

Except for the reports by Debrie[26] and Briggs[27] these are the only papers I have been able to find in which the attempt is made to prove that the milder forms of typhoid fever have often been concealed under the names simple continued fever, mountain fever, etc. A number of papers have been written in which the authors express the belief that short-duration typhoid fever is of common occurrence and often overlooked, but they either offer no proof or relate only one or two cases.

No paper has yet been published on the bacteriology of the blood in the milder forms of typhoid fever. Buxton and I[28] analzyed the reports of 1602 cases whose blood had been examined bacteriologi-

[18] Soc. méd. d. hôp. d. Paris, 3s, xiii, 669.
[19] Ibid., 1896, 3s,, xiii, 698.
[20] Arch. d. méd. et pharm. mil., 1897, xxx, 313.
[21] Ibid., 1898, xxxii, 102.
[22] Jour. Amer. Med. Assoc., 1898, xxx, 753.
[23] Centralbl. f. Bakt., 1903–04, xxxv, 1 Abt., 776.
[24] Quoted by Talayrach, Arch. d. méd. et pharm. mil., 1903, xlii, 393 (unable to find original reference).
[25] Jour. Amer. Med. Assoc., 1909, lii, 1903.
[26] Arch. de la Direction du service de santé du XIV Corps d'Armée, 1902.
[27] Amer. Med., 1904, viii, 639.
[28] Amer. Jour. Med. Sci., 1907, cxxxiii, 896.

cally, and the only reference we found to the subject was a brief paragraph by Conradi[29] stating that he had recovered the typhoid bacillus twice from the blood of cases lasting about eight days each.

THE BELLEVUE HOSPITAL CASES. We do not see many of the milder forms of any disease in Bellevue Hospital. Nevertheless, in the last five years, exclusive of 1908, 10 per cent. of 229 cases of typhoid fever on the second medical division have been of the short-duration variety. The proportion of mild to severe cases has varied in different years: thus, in 1903 there were only 2 mild cases; in 1904, 11 cases (constituting for that year 25 per cent. of the typhoids); in 1905, 4 cases; in 1906, 5 cases; and in 1907, 2 cases. The febrile period in 9 of the 24 cases lasted about two weeks, in 9 it lasted ten days, in 4 it lasted nine days, and in 2 cases it lasted five and six days respectively. One of the two cases which occurred in 1903, and which lasted nine days, gave Bacillus coli in pure culture in the blood, but I think it may with propriety be included here.[30] The diagnosis in 20 of the 24 cases is not open to doubt, since it rests either upon a positive serum reaction or upon a positive blood culture. In the remaining 4 cases the diagnosis was made upon clinical evidence, it having been impossible for various reasons to study the cases thoroughly, and it therefore is doubtful.

The serum reaction was negative in 6 cases of the series, but in 2 of these the typhoid bacillus was obtained in pure culture from the blood. In 3 of the negative cases blood cultures were not made. In the remaining negative case a blood culture in broth was also negative.

Blood cultures were taken in 19 of the 24 cases, with a positive result 9 times and a negative result 10 times. In one of the negative cases the blood was not taken until after the temperature had reached normal, and according to our present experience would not be expected to contain the bacilli. The bacillus was not found in the blood in any case of less than nine days' duration. Conradi's bile medium was used in only two of the negative cases, the other negative cases having been studied before this medium was recommended. As we have had about 97 per cent. of positive results with the bile medium in all varieties of typhoid fever, and have been much less successful with broth, we do not feel that the negative cases in which broth was used are entirely reliable.

Symptomatology. The symptoms of short-duration typhoid fever have been so well described by several authors, notably Curschmann,[31] that I shall not discuss them. The temperature curves (Figs. 1, 2, and 3) will show in a general way the course of several of the Bellevue cases.

[29] Deut. med. Woch., 1906, xxxii, 58.
[30] AMER. JOUR. MED. SCI., 1909, cxxxvii, 199.
[31] Nothnagel's Encyclopedia, Typhoid fever.

Diagnosis. If one may judge of the attitude of the medical profession toward short-duration typhoid fever from current literature and text-books, the conclusion must inevitably be reached that these cases are not often recognized.

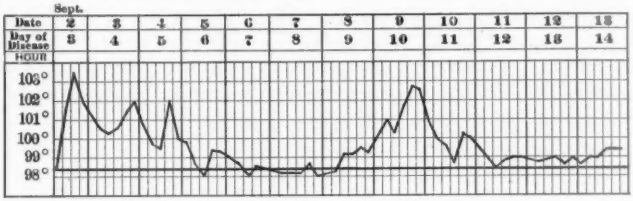

FIG. 1.—Herman R., typhoid fever of seven days' duration, with relapse; positive typhoid serum reaction; blood culture negative.

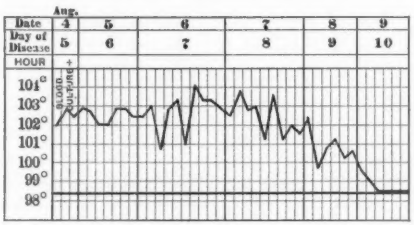

FIG. 2.—Terence B., typhoid fever of ten days' duration; typhoid bacillus obtained from the blood.

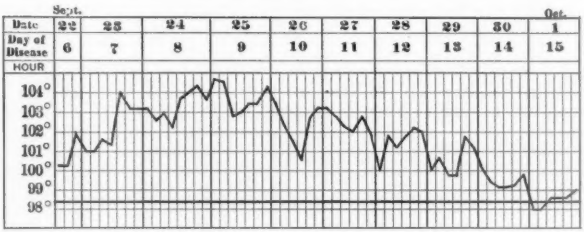

FIG. 3.—Dennis C., typhoid fever of fourteen days' duration; typhoid bacillus obtained from the blood.

Reed, Vaughan, and Shakespeare[32] state their belief "that the number of cases of typhoid fever among the troops of the —— and —— Army Corps was more than twice the number recognized as having that disease." And after a discussion of the mortality statistics of typhoid fever in several of the larger cities of the

[32] Report of the Commission appointed by the President to investigate the conduct of the War Department in the war with Spain. Washington, 1899, pp. 59, 61.

country, they say:[33] "We are forced to conclude that in these cities a large percentage of the cases of this disease are not recognized as typhoid fever. The army surgeon did in his military service just as he was in the habit of doing in his civil practice, *i. e.*, he failed to properly diagnosticate the milder cases of typhoid fever. His military record is no worse and no better than was his own record in civil practice or is the record of physicians in some of the largest cities of the United States." The sweeping character of this indictment is startling, but the review of the literature forces the admission that it is not overdrawn. Moreover, this review also shows that the failure to recognize the shorter forms of typhoid fever has not been confined to any one country, but has been world-wide.

Lafforgue[34] says of short-duration typhoid fever: "The true nature of these forms is not often recognized. They constitute one of the most formidable sources of infection."

Turning to the standard text-books, it is found that all of them contain descriptions of the classical case of typhoid fever, with the usual division of the disease into three periods of a week each. Most of them speak of the abortive cases which begin as the longer cases do. Only one of the American text-books gives more than a passing notice to cases which last less than two weeks. Curschmann gives a classical description of these cases, while Dreschfeld says of them only that during epidemics of typhoid fever, when many mild and abortive cases are about, the differential diagnosis from acute gastro-intestinal catarrh may present great difficulty—and leaves the means of overcoming the difficulty to the reader's imagination. The strongest impression conveyed by the text-books is that typhoid fever is a disease of three weeks' duration.

As a final quotation, bearing upon the diagnosis of short-duration typhoid fever, I may cite the title of a paper, by an experienced physician, which appeared in February, 1908. His title is the question, "Is there such a disease as abortive typhoid?" The author believes that there is, but adduces no proof.

When one considers the state of confusion which still exists, according to the published opinions of the leaders of the medical profession, concerning the milder forms of typhoid fever, and also the fact that the study of these cases with the aid of the newer laboratory methods has been largely neglected, it is not surprising that practical physicians should hesitate to make the diagnosis of typhoid fever in a case which shows few of the classical symptoms of the disease and which completes its course in two weeks or less. In a recent conversation with a progressive physician from a town of about 12,000 inhabitants, he said he would be disposed to think

[33] Ibid., page 61.

[34] Arch. gén. d. méd., 1905, ii, 2625, 2635.

he had made a mistake in diagnosis if a supposed case of typhoid fever lasted less than two weeks.

But the diagnosis of these cases may easily be made in general practice. It cannot be made clinically except in the presence of some typical complication; one must have recourse to laboratory methods. With dead cultures of the typhoid bacillus, which may be obtained in the market, the serum test may be carried out by any busy practitioner.

Serum Reaction. The fact is well known that a patient's serum may give a positive reaction to the typhoid bacillus when the patient is not suffering from typhoid fever. A positive typhoid reaction means only that the bacillus is growing in the body, and that immune bodies (agglutinins) are forming. Cases of typhoid infection of the biliary passages and typhoid bacillus carriers furnish examples. But if a positive reaction appears transiently during the course of a febrile attack, which is not obviously due to some other cause, the diagnosis of typhoid fever is reasonably certain. It need scarcely be added that to be of value the serum tests must be carefully performed and properly controlled.

The sera of cases of infection by the intermediate members of the typhoid-colon group (the paratyphoid and paracolon bacilli) and by Bacillus coli react only exceptionally to the typhoid bacillus, and should be tested against these organisms. So far as is known at present, however, cases caused by these bacilli constitute but a small proportion of the total typhoids, and except in special instances may be left out of consideration. But it must not be forgotten that epidemics of typhoid fever have been caused by the paratyphoid bacilli (Friedel,[35] Lempke, Schottelius,[36] Kutscher[37]).

Negative serum reactions possess no diagnostic value unless they are obtained daily throughout the febrile period of the disease and well into convalescence. In some of the Bellevue Hospital cases agglutinins were present in the blood for only one or two days, and if the reactions had not been tested on those days the results might have been considered negative throughout.

Bacteriological Examination of the Blood. Bacteriological examinations of the blood cannot be made unless one has access to a well-equipped laboratory, and therefore will not be of much assistance in diagnosis to the general practitioner. However, the method has served the useful purpose of setting at rest all doubt concerning the occurrence of short-duration typhoid fever. According to our experience at Bellevue, the typhoid bacillus is not found in the blood as uniformly in the short-duration cases as in the longer and severer forms of the disease. In several instances as many as three examinations of the blood gave negative results. Positive bacterio-

[35] Zschr. f. Med-Beamte, 1905, xviii, 306.
[36] Münch. med. Woch., 1905, lii, 2116.
[37] Ztschr. f. Hyg. u. Infktskrankh, 1906, lv, 331.

logical examinations of the stools and urine do not necessarily prove that the patients have or have had typhoid fever. Brown[38] has reported a case of cystitis, caused by the typhoid bacillus, in a patient without a history of typhoid fever. And bacilli of the typhoid-colon group are not infrequently found in the stools of healthy persons —witness the bacillus carriers.

In conclusion, I would say: This study has proved in an incontestible manner that some, at least, of the fevers which formerly would have been considered febricula or simple continued fever are in reality typhoid fever. In the present state of our knowledge it would be rash to assert that all mild fevers in this latitude, for which no other cause can be found, are typhoid in nature, but I can state that we have had no series of cases of mild fevers in Bellevue Hospital in the last five years which could not be proved to be either typhoid fever or some easily recognized disease, as bronchitis, gastro-intestinal disturbance, etc.

This investigation has also brought out the fact that a great deal of confusion exists in the literature concerning the milder forms of typhoid fever, and emphasizes the urgent need, from the epidemiological standpoint, of a more thorough study of these forms. No statistics have been accumulated, since exact methods of diagnosis have come into general use, to show the relative proportion of the mild to the severe cases of typhoid fever. Doubtful cases should be treated as typhoid fever until the cause of the disease can be found.

I would suggest that unless the writers of text-books on medicine, from which students are taught and to which practitioners turn when in doubt, devote more attention to the consideration of the milder forms of typhoid fever, they cannot hope to escape responsibility for a large share of blame for the occurrence of epidemics arising from this source.

Finally, I wish to express my indebtedness and my thanks to Dr. Buxton for making the blood cultures and to Dr. Hastings for performing the serum tests.

HEART FAILURE IN INFECTIOUS DISEASES: ITS PREVENTION AND SUCCESSFUL MANAGEMENT.

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of New York.

Thoroughly to understand the management of infectious fever it is necessary that we understand what is blood pressure, the cause of its enfeebleness, and the proper method to be adopted for its

[38] Johns Hopkins Hosp. Rep., 1901-02, x, 11.

control. Blood pressure is a misnomer. The blood does not press upon anything: it is the blood being pressed upon by the three chief blood pressures: (1) The pressure behind the column, the force of the heart; (2) the pressure on the sides of the column, the normal contraction of the muscular fibers of the arteries, and the elastic fibers of the arterioles; and (3) the resistance at the head of the column, the normal elasticity of the capillary bloodvessels. These pressures are maintained wholly by the nerve centres in the medulla oblongata and are enfeebled according to the intensity of the infection and the toxic effects upon those centres. If one of these pressures is relaxed a relaxation of the other two occurs.

Heart failure, that demon whom every intelligent and painstaking physician fears, stands by the bedside of every patient suffering from infectious fever. This enfeebleness of the heart arises from a relaxation of the vasomotor nerve centres by reason of which the capillary vessels lose their elasticity and normal tone. Winternitz has demonstrated in the circulation of the frog that loss of tone and diminution of tension of the capillary vessels enfeebles the action of the heart. Loss of tone then and diminished tension are the cause of heart failure. In infectious fever the danger lies not in the heart but in the toxemia which is spending its full force upon the nerve centres and thus impairing the functions of the organs dependent upon them. Cardiac action, secretions, and nutritional processes are all being crushed by the octopus infection, but the cold bath comes to the rescue, or any form of application of water, according to the indications of the case, when properly applied. The nervous system is refreshed, the eye brightens, the mind clears up, the inspiration deepens, the pulse is slowed and rendered less dicrotic. I distinctly remember two cases of my early days of practice, one of diphtheria, in a child aged thirteen years, and one of typhoid fever, in a subject aged thirty-five years, that were getting well, as I thought; the temperature was normal and the pulse about normal but weak, and both patients were bright; both of them died very suddenly of paralysis of the heart. These were prior to 1889. During that year I took up the study of hydrotherapy in its every phase.

The treatment of the aforementioned cases was by the expectant plan, a term well named, for always something was expected to happen which the physician was powerless to avert. As Dr. Beverley Robinson[1] has justly said, "No organ of the body more frequently requires our wisest government than the heart;" but I would like to add on that point, no organ obeys better than the heart when ordered to do so by the proper authority. An employee who would not obey the command of another employee (strychnine, nitroglycerin, strophanthus, alcohol, digitalis, musk, or other drugs) will obey the command of the boss when he has been reported as negli-

[1] AMER. JOUR MED. SCI., 1908, cxxxvi.

gent of duty. The employee who is ordered in this instance is the heart, and the boss is the central nervous system which controls it and whips it into proper service by means of cold applied to the peripheral nerve terminals. A patient desperately ill with low muttering delirium, unconscious of her surroundings, jactitation, and continually rolling around the bed, whom I saw lately, was completely restored to health by the "general ablution" which I have so often described. This patient's mind was a perfect blank, she did not know her own immediate relatives, nor when her daughter carried her in her arms to the bath tub for three successive days. This patient took "general ablution" at 70° every four hours for about a week, and one "affusion" and one "drip sheet," and was out walking and exercising in the open air inside of ten days.

The excitation of cold is the most valuable, powerful, and reliable stimulant when properly applied, and accomplishes many other important indications. The nerve centres are gently stimulated by the successive gentle shocks of the cold, according to the hydriatic prescription and subsequent reactive stimulus to the sensory fibers of the skin, which is conveyed to the central nervous system and thence reflected to all the functions over which it presides, and upon whose functionating capacity depends the patient's ability to withstand the toxic agents circulating in the blood. In this manner is cardiac action maintained. The several methods of procedure are interesting: for instance, in weakly patients "ablutions" are found most useful. Each part of the body in these cases may be successively bathed, first wrapping the part in a long-haired blanket for one hour, then washing down with water at 88° to 92°, beginning with the higher temperature with good friction, light or coarse, and reducing 2° each ablution to 70°, according to the reactive capacity of the patient, until the whole body has been gone over, chest, back, arms to elbows, and thighs to the knees, with a minimum of disturbance to the patient and a most refreshing effect. This is when the patient is in bed and cannot get up. Dilatation of the capillary vessels always follows friction, which must never be omitted, as it is the sine qua non of all applications of cold water. Chilling of the patient and a little chattering may sometimes occur, but there is nothing at all to be feared from it, as these baths generally reduce the temperature 2° or 3°, deepen the breathing, stimulate the heart, and refresh the patient as no remedial agent is capable of doing. In order that its effect be continuous upon the heart it is necessary that the operation be repeated every three hours. The most important effect of these applications is the aid and sustenance they afford the central nervous system, which bears the brunt of the fight, stimulating it to enhance the vital powers of the patient and thus place him on the road to a rapid recovery.

Management of the patient by means of hydrotherapy renders the prognosis of the case entirely different from management by the expectant plan. Recovery by the expectant plan seems to depend

upon circumstances over which the physician has no control; if the patient has the constitution to withstand the toxemia he gets well; if not, he dies; but by hydrotherapy we enhance the patient's vital powers against the lethal agencies evolved in the infection process, thereby spurring on the central nervous system to furnish innervation for respiration, circulation, digestion, tissue building, and excretion, and bridging over the danger which would arise from failure of these functions.

THE SYMPTOMS OF DESCENDING THORACIC ANEURYSM.

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Aneurysms of the thoracic arch which reach any considerable size usually produce characteristic signs or symptoms. An abnormal pulsation, murmur, or area of dulness, a tracheal tug, or a left vocal paralysis immediately direct attention to the possible presence of an aneurysm, and the *x*-rays are called upon to contribute their important diagnostic aid. When the descending thoracic aorta is involved, however, signs and symptoms are very apt to be lacking, and when present they are frequently misinterpreted. In the cases that we have seen this has occurred almost uniformly. It seems advisable, therefore, to report our cases, calling special attention to the typical pains that have been so graphically described by Huchard.[1] Autopsies were obtained in but two of our six patients, yet the diagnosis in the remainder was made almost certain by the results of *x*-ray examination.

Case I.—W. T. H., a stableman, aged forty-two years, was first seen at the Cooper Medical Dispensary, San Francisco, on June 5, 1903, complaining of pain in the left side. The family history was negative. The patient had had the ordinary diseases of childhood, grippe in 1887, and gonorrhœa three or four times. He denied syphilis, but had always chewed tobacco and drank excessively. Since October, 1902, he had suffered from pain in the left side of the thorax, which was worse at night and kept him from sleeping. At times he had slight dyspnœa.

Examination showed a well-nourished man with a face indicative of overindulgence in alcohol. The pupils were equal and reacted normally. Both sides of the chest expanded poorly, but the left distinctly less than the right. The breath sounds were feeble and

[1] Maladie du cœur et de l'aorte, ii, 427.

distant, the expiration prolonged. No abnormal dulness or bruit over the back, and no friction sounds were found. The area of cardiac dulness was enlarged moderately to the right and left. The heart sounds were normal in character and intensity. The pulse was 110, equal and synchronous in both wrists. The radial arteries were moderately thickened. There was no tracheal tug.

On account of a distinct tenderness along the course of the fifth and sixth intercostal nerves a diagnosis of intercostal neuralgia was made and the ordinary remedies given. The patient returned occasionally to the dispensary for several months, always with the same complaint of pain in the left side. Repeated examinations by different members of the staff failed to discover any sign that would

FIG. 1.—Skiagram of Case I.

indicate the cause of the pain other than the tenderness over the nerves. After a few months the patient ceased coming to the dispensary.

On March 8, 1905, he returned again, complaining of his old symptoms. Again the examination was negative, except for very definite tender points to the left of the spinal column, in the left axilla, and to the left of the sternum. On account of the severity of his pain, he was sent to the Lane Hospital and was again treated for neuralgia. On April 6, 1905, a routine fluoroscopic examination was made by Dr. Lehmann. His note in part was as follows: "The transparency of the left lung is markedly less than that of the right. In the left side of the thorax there is a large shadow about the size of a child's head, which cannot be differentiated from the shadow of the

aortic arch. This shadow is sharply outlined and apparently shows true pulsation. Viewed from behind, the shadow is more marked, clearer, darker, and smaller than when viewed from the front. The heart is in a pronounced horizontal position. The diaphragm on the right side moves 6 to 7 cm., on the left side only 3 to 4 cm." In veiw of these findings (Fig. 1), a diagnosis of aneurysm of the descending thoracic aorta was made. Two days later the patient began to cough up blood, and died within a few minutes.

The autopsy, performed by Dr. Ophüls, showed the heart to be normal. There was marked atheroma with many white retracted scars and moderate dilatation of the proximal portion of the aorta; less dilatation of the arch. At the distal end of the arch posteriorly a round opening about 4 cm. in diameter lead into an aneurysmal sac about the size of an apple. The aneurysm extended posteriorly and to the left, and had deeply eroded the spinal column. The aneurysm was adherent to the left lung, and had perforated into the upper posterior part of the lower lobe, which showed hemorrhagic infiltration. The lower thoracic and abdominal aorta showed very little atheroma.

Case II.—C. W., aged sixty-one years, a veteran, came to the Cooper Medical Dispensary on January 3, 1908, complaining of stomach trouble. The family history was unimportant. The patient had always been strong and healthy. He had had jaundice in 1880, pneumonia in 1890, and a hard chancre about 1890, not followed by secondaries. He was treated with mercury and potassium iodide. He had had several attacks of gonorrhœa. He never drank excessively. His present illness had begun five or six months before with a boring pain in the back. This pain had been more or less continuous and had often prevented his sleeping. About six months ago his stomach had begun to give him trouble for the first time. He suffered from epigastric pain, which seemed to be made worse by eating. He had vomited occasionally, but never vomited blood or material eaten on previous days. There was no difficulty in swallowing, and no jaundice, cough, or headache. There was slight dyspnœa on exertion. He was very constipated. He had lost 70 pounds in six months, and was very weak.

Examination showed an emaciated, pale, old man. The pupils were equal and reacted normally. The lungs were negative. There was moderate dilatation of the cutaneous veins across the upper left front of the thorax and left shoulder. Careful examination posteriorly and anteriorly failed to show any definite abnormal pulsation, dulness, or bruit. There was no tracheal tug. The heart was negative. The liver was slightly enlarged and palpable. There were no enlarged glands. Inflation of the stomach showed no dilatation. No abdominal tumor was felt either externally or by the rectum. The urine was negative. The blood showed a marked secondary anemia: red corpuscles, 3,750,000; hemoglobin, 66 per cent.; leuko-

cytes, 8000, with a normal differential count. The stomach analysis showed an absence of free hydrochloric and of lactic acids; total acidity, 10; no retention of raisins taken the night before.

In this patient the recent onset of serious stomach trouble at the age of sixty-one, the rapid loss of weight, the secondary anemia, and the results of the stomach analysis led us to suspect a gastric carcinoma. The thoracic pain and the dilatation of the veins over the upper left chest and shoulder aroused a strong suspicion of metastases into the posterior mediastinum. An *x*-ray plate was therefore taken. Though rather poor and taken too low down, this sufficed to show a uniform round shadow above and to the left of the heart shadow (Fig. 2), characteristics which in connection with the

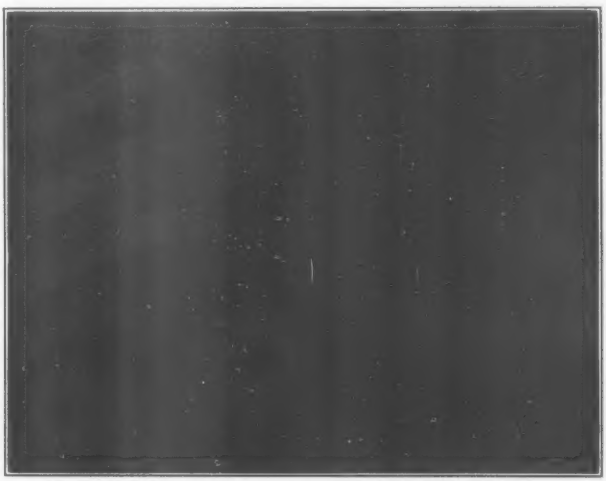

FIG. 2.—Skiagram of Case II.

symptoms led us to a diagnosis of an aneurysm of the descending thoracic aortic. As the patient left the city immediately after his exposure to the *x*-rays, it was not possible to reëxamine him. He died on January 27, 1908. The autopsy, performed at the Veterans' Home, Yountville, by Dr. A. H. Reinstein, showed that the cause of death was the rupture of an aneurysm of the descending thoracic aorta into the left pleural cavity. A carcinoma of the pylorus with metastases in the posterior lymphatic glands were also found.

CASE III.—C. A. B., aged fifty-one years, a paper hanger and decorator, entered the Lane Hospital on January 27, 1908, complaining of pain under the lower left scapula and in the epigastrium. The family history was negative except for the death of two brothers of tuberculosis. He had always been strong and healthy, never having

had any of the acute infectious diseases since childhood. He had been a periodic drinker and had smoked excessively. He had gonorrhœa once. At twenty-one years he had what appears to have been a soft chancre without secondaries. The present trouble had begun about a year before, with constipation and dyspepsia. This had lasted a few weeks, then disappeared for a few months, and recurred for a few weeks. Three months ago the dyspepsia, constipation, and pain in the epigastrium had re-appeared, and have been present more or less continuously up to the time of admission. The pain had gradually grown worse. It was most marked in the epigastrium, but sometimes extended through to the left back. When the pain was severe the epigastrium was rather tender and felt drawn, as if a

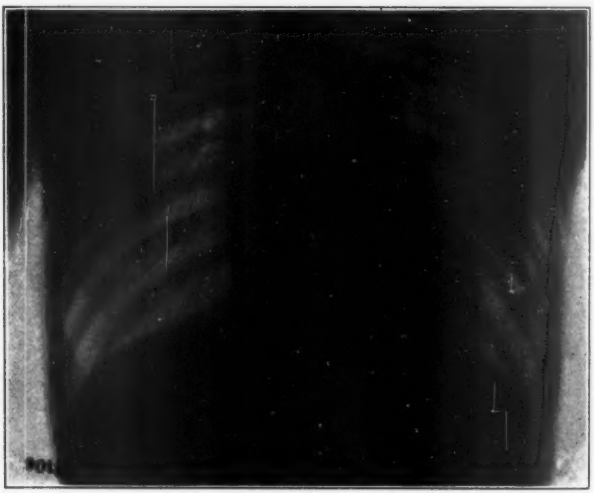

FIG. 3.—Skiagram of Case III.

lump were present there. At times the pain was accompanied by belching of gas. The pain showed no definite association with the taking of food. It was most marked when the patient lay down or when he sat too long in one position. It was most severe at night, and often wakened him out of a sound sleep.

Examination showed a well-developed but rather poorly nourished man. The pupils were equal and reacted normally. The lungs and heart were negative. There were no normal pulsations, no dulness, and no bruit over the back. Both sides of the chest moved symmetrically. Abdominal examination was negative, except for a slight rigidity of the upper left rectus muscle, which became more marked when the pain was severe. The urine and blood were normal. Repeated examinations of the feces for occult blood were negative.

Two stomach analyses gave approximately identical results: 60 c.c. of yellowish mucoid material, containing bits of undigested bread; total acidity, 18; no free HCl, no lactic acid, no occult blood, no retention of raisins taken the night before.

The pains were not relieved to any appreciable degree by careful dieting and the administration of acid. During his stay in the hospital they gradually became more severe, especially posteriorly at about the level of the tenth dorsal spine. The only circumstance which seemed to influence them definitely was posture. Whenever he lay on his back or left side the pains became worse. For this reason he usually slept lying face downward. Considerable tenderness to deep pressure was discovered over the eighth to eleventh dorsal spines. A zone of hyperalgesia to the scratch of a pin was found on the left side corresponding to about the distribution of the ninth and tenth dorsal nerves. This hyperalgesia was much more marked behind than in front. On account of the hyperalgesia and the effect of posture upon the pains, an *x*-ray plate was taken of the lower thorax (Fig. 3). This showed an abnormal shadow behind the heart apparently continuous with the shadow of the descending thoracic aorta. Dr. C. M. Cooper[2] agreed with us that the symptoms and *x*-ray examination taken together indicated that the patient was suffering from an aneurysm of the descending thoracic aorta.

Case IV.—O. K., aged thirty-eight years, a butcher, came to the Cooper Medical Dispensary on March 23, 1908, complaining of pain over the heart and between the shoulders. The family history was negative. While serving in the German army, at sixteen years he contracted gonorrhœa and at the same time had a chancre, followed by definite secondaries. He was treated with inunctions. He had been a hard drinker and a moderate user of alcohol. His present illness had begun three months before with pain over the heart and between the shoulders. These pains were very intense. They came on only when he lay on his back or on his left side, and not, as a rule, when he lay on his abdomen or right side. The pain was not influenced by exertion, coughing, or deep respiration. About one-half hour after lying down, he would be wakened by the pain, and relief could only be obtained by sitting up for a few minutes. If he again lay on his back, the pain invariably returned. He had had slight dyspnœa for fifteen years. There was no swelling of the feet, no cough, and no loss of the voice; appetite was good; the bowels were regular.

Examination showed a well-nourished and healthy-looking, though somewhat nervous, man. The pupils were equal and reacted normally. An indefinite tracheal tug could be felt when he lay recumbent and held a deep breath. The left side of the chest moved decidedly less than the right. There was no definite dulness, respira-

[2] We are indebted to Dr. Cooper for this plate, as well as those of Cases II and IV.

tory changes, or bruit over the back. The heart was negative, except for a moderate accentuation of the second aortic sound. The radial arteries were moderately thickened. There was no tenderness over the dorsal spines. An area of hyperalgesia to the pin scratch could be easily demonstrated to the left of the vertebral column, extending in a vertical direction from about the fourth to the eighth dorsal spines and laterally as a band around the left side of the chest (Fig. 4). This hyperalgesia was much more marked behind. In front it became narrower and less definite in outline. On account of the history of syphilis, the accentuation of the second aortic sound, the area of hyperalgesia, and the character of the pain, a probable diagnosis of aneurysm of the descending thoracic aorta was made. This was confirmed by flouroscopic examination, which showed a large pulsating shadow to the left of the spine, more distinct when viewed

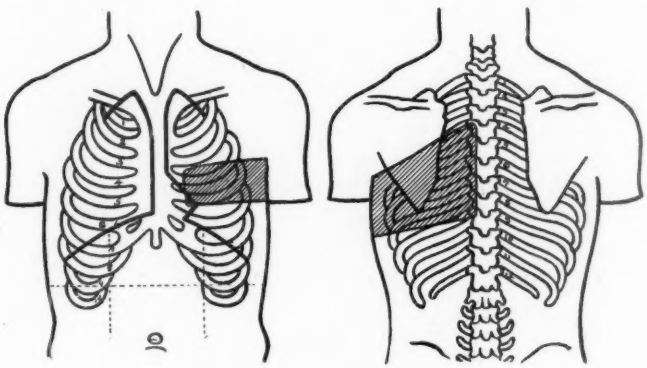

FIG. 4.—Hyperalgesic zone in Case IV.

from behind than when viewed from the front, and plainly located in the back of the chest when the patient stood in an oblique position (Fig. 5). An aneurysm of the descending thoracic arch was, therefore, the cause of this patient's pain.

CASE V.—J. G., aged forty-one years, entered the medical ward of the University of Michigan Hospital on October 10, 1908, complaining of shortness of breath and of constant pain in the left side of the abdomen and back. The family history and past history were negative. He denied alcoholic excesses and venereal infection. The present trouble began about three years before with sharp pains in the left side, which lasted three days and were relieved by a lotion. After a couple of weeks the pains again returned and were again relieved by rubbing. These pains had continued off and on and with varying intensity since then. About a year before they had been so severe that he could not sleep for six weeks. They had been diagnosticated

as pleurisy and intercostal neuralgia. He had also been moderately short of breath on exertion, and at times had suffered from palpitation.

In the ward the patient was usually found on his left side, which position afforded him relative relief from his pains. His pupils were equal and reacted well on accommodation, but not to light. There was no tracheal tug. The left chest lagged on inspiration, especially in its lower part. There was some impairment of resonance over the left lower chest behind, from about the sixth spine down, accompanied by diminished breath sounds. Indefinite systolic pulsation was noted on some occasions just to the left of the eighth spine. Below this a fair Broadbent sign could be seeen at times. Over the area of pulsation the heart sounds were heard exceptionally well, but there were no murmurs.

FIG. 5.—Skiagram of Case IV.

The apex beat was rather diffuse, but could be distinctly felt as far as 14.5 cm. to the left of the median line in the fifth intercostal space. In the recumbent posture a systolic thrill was felt in the third left intercostal space. The area of cardiac flatness was decidedly enlarged, extending from the middle of the sternum to within 1 cm. of the left mammary line. It joined the liver flatness by an obtuse angle. The area of cardiac dulness extended 15 cm. to the left of the median line and 5 cm. to the right. It was continuous above with a broad area of dulness, which extended upward on either side of the sternum to the clavicle. At the apex one heard a slight blowing systolic murmur and an indefinite diastolic rumble, the latter being sharply limited to the region of the apex beat. Toward the sternum

the systolic murmur became louder, reaching its maximum in the third intercostal space 5.5 cm. from the median line. Here it was an exceedingly rough and intense murmur. This murmur was transmitted over the left chest upward as far as the second rib and outward as far as the anterior axillary line. It was barely heard beyond the right border of the sternum and not heard in the vessels of the neck. It was faintly heard over the left back opposite the second dorsal spine. In front the murmur became less loud during deep inspiration and when the patient sat up. It varied in intensity from time to time, but, on the whole, was very constant. The pulmonary second sound was accentuated and at times could be felt as a distinct shock. The knee-jerks and ankle-jerks were absent. The urine and blood were negative.

One of the most striking features of the patient's examination was the zone of disturbed sensation which extended around the left side

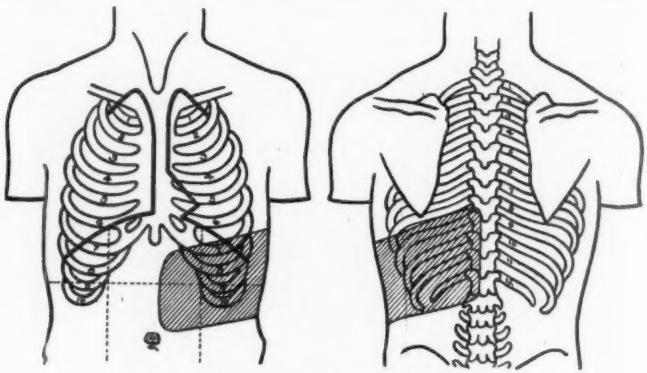

FIG. 6.—Hyperalgesic zone in Case V.

from the spine to the median line in front. It varied in width, but was most constant between the levels of the eighth and twelfth dorsal spines behind and the ensiform and umbilicus in front (Fig. 6). At first there was everywhere extreme hyperalgesia to the pin scratch and to pressure, but later the anterior portion of the zone showed anesthesia to the touch of the camel's-hair brush and was associated with hyperalgesia to the pin scratch. On November 29 a slight weakness of the upper left rectus muscle was noted, but this later became less marked.

During his stay in the hospital the patient suffered more or less continuously from pain in the left side. When this was severe he always lay on this side, other positions being impossible on account of pain. When the pain was less severe he occasionally walked about the ward, but one gained the impression that such exertions were often succeeded by renewed exacerbations of the pain.

FIG. 7.—Skiagram of Case V taken in a sagittal direction.

FIG. 8.—Skiagram of Case V taken from the oblique position; it shows the left aneurysmal border distinct from the heart.

The *x*-ray examination showed an abnormal shadow behind the heart. If the patient, facing the flouroscopic screen, were rotated to the right, this abnormal shadow could be seen moving to his left while the heart moved to his right, thus demonstrating its position behind the heart. Plates taken from two directions (Figs. 7 and 8). illustrate this. The smooth rounded outline of this posterior shadow, together with some pulsation, indicated that it was caused by an aneurysm of the descending thoracic aorta situated behind the heart. The crowding of the heart forward undoubtedly accounted for some of the abnormal cardiac signs and rendered it difficult to determine

FIG. 9.—Skiagram of Case VI.

just what other factors came into play, though probably the loud systolic murmur over the pulmonary area was due to a partial obstruction of the pulmonary artery or its left branch. The patient had tabes dorsalis, and one might question whether his pains and disturbed sensation were due to the aneurysm or to the tabes. As the site of these nervous disturbances corresponded to that of the aneurysm, it seems probable that the latter was their cause.

CASE VI.—W. B., aged sixty-four years, had entered the medical ward of the University of Michigan Hospital on several occasions suffering from arteriosclerosis, dilated heart, and chronic nephritis. He had the ordinary symptoms of broken compensation together

with Cheyne-Stokes breathing. The discovery of his aneurysm was purely accidental. A plate taken to determine the heart outlines showed a rounded shadow which arose from the middle shadow at the upper level of the aortic arch and described an arc well outside the left sternal margin until it intersected the heart shadow (Fig. 9). Fluoroscopic examination of this abnormal shadow showed that it pulsated, and by rotating the patient on a revolving stool, that it was situated in the posterior portion of the chest. It was more clearly seen from behind than from in front. The patient showed no deformity of his chest. We must conclude that this was a fusiform aneurysm of the descending thoracic aorta. Apparently it produced no symptoms whatever. Neither could signs be found which were definitely referable to the aneurysm, with the possible exception of bronchovesicular breathing in the left axilla. This might have been due to compression of the lung.

A review of these six cases of descending thoracic aneurysm allows us to divide them roughly into two groups. In the first, which is represented by the first five cases, the main symptom was pain; in the second group, represented by the last case, no symptoms whatever were present. There are numerous instances in the literature of the accidental discovery of unsuspected aneurysms. This occurred in 5 per cent. of the 104 aneurysms reported by Baetjer.[3] It happens so frequently when the aneurysm arises from the descending thoracic aorta that Huchard[4] speaks of this as the zone latente des aneurysmes meconnus, des erreurs de diagnostic. Such aneurysms may reach a large size without giving rise to any symptoms previous to their final rupture into the lung, bronchus, esophagus, pleural cavity, or mediastinum.

The remaining five cases may be grouped together, the main symptom being pain. In our patients this pain, though varying from time to time, was, on the whole, of extraordinary severity. Its situation in the individual patient was practically constant, and it was remarkably resistant to all forms of medication. In one patient the pain was of a dull, boring character and located in the centre of the back. In the other four it was limited to the left side of the thorax and was of a neuralgic type, with either typical tender spots or a zone of cutaneous hyperalgesia. The latter was present in three patients, and in one of these (Case V) it was associated at times with anesthesia to the touch of the camel's-hair brush. Such a dissociated sensory disturbance caused by the pressure of an aneurysm upon the intercostal nerves has been described in detail by Frick.[5] In one of our

[3] The *X*-ray Diagnosis of Thoracic Aneurysms, Johns Hopkins Hospital Bulletin, 1906, xvii, 24.

[4] Loc cit, p. 413.

[5] Ueber objective nachweisbare Sensibilitätsstörungen am Rumpfe bei Aneurysma Aortæ, Wien. klin. Woch., 1901, No. 25.

patients there was a spasm of the upper left rectus muscle, which increased when the pains were severe; in another there was at times a paresis of this muscle. In all the cases of this group the pain showed pronounced nocturnal exacerbations. In three this was a distinctly postural effect, for the pain was accentuated when the patient lay on his back. One patient slept on his face, another on his left side, while a third had to sit up in order to be relieved of the pain. In two of our patients the main pain was referred to the front of the body; in Case IV, to the heart, simulating angina pectoris, and in Case III, to the upper abdomen. Such referred pain may lead to the mistaken assumption that a viscus is diseased and that the tenderness or hyperalgesia behind is a Head's area. Thus, in Case III, with epigastric pain, spasm of the left rectus muscle, and tenderness behind, it was at first believed that the pain originated in the upper abdomen. This patient had been sent into the hospital for an exploratory operation, which might have been performed in the attempt to locate the pain had not the *x*-ray examination demonstrated an inoperable condition. Similar pseudogastric pains have been noted by others (Rendu[6]); and Baetjer recites a somewhat analogous history of a patient in whom a gallstone operation had actually been performed with negative findings three years before the *x*-rays finally showed that a large aneurysm of the descending thoracic aorta was the cause of symptoms. Milanoff[7] found histories of three patients who had been treated for renal colic. These abdominal pains are particularly apt to be caused by aneurysms situated just above the diaphragm. They are common enough also in abdominal aneurysms. A patient recently sent into the Lane Hospital was supposed to be suffering from biliary colic or a duodenal ulcer, but the exploratory operation showed an aneurysm of the upper abdominal aorta.

The neuralgic pains present in four of our patients were evidently due to some damage to the intercostal nerves. Whether they were due to pressure alone or, as many clinicians believe, to a chronic inflammation in the neighborhood of the aneurysmal sac is difficult to decide. The pain referred to the front of the body, the zones of disturbed sensation, and the spasm or paresis of the muscles evidently could not be accounted for by other factors sometimes held responsible for aneurysmal pains, such as erosions of the bone or disease of the vessel wall.

From our experience pain is the most frequent symptom of descending thoracic aneurysm. Milanoff, who collected the histories of 120 patients with this disease, found pain mentioned in 72 of them, whereas dysphagia occurred in 20, hematemesis in 13, hemoptysis in 21, left pleural effusion in still fewer. Andréef[8] could collect but 8

[6] Cited by Milanoff.

[7] Etude de la douleur et de quelques autres symptomes des anévrismes de l'aorte thoracique descendante, Thèse de Paris, 1900.

[8] Contribution à l'étude des anévrismes de l'aorte descendante, Thèse, Toulouse, 1904.

cases of paraplegia from this cause. When one remembers that most of these symptoms, with the exception of pain, occur late in the disease, the great importance of pain as an early symptom of descending thoracic aneurysm becomes apparent. In some instances it has lasted ten or even twenty years.

The physical signs of aneurysm of the descending thoracic aorta are of such an indefinite character that only exceptionally can one make a diagnosis from signs alone previous to erosion of the bony thorax. In none of our patients was a murmur heard over the site of the aneurysm, though listened for in every case. In Case V, in which a large aneurysm was situated directly behind the heart, the heart sounds were heard with unusual distinctness over the site of the aneurysm. Slight pulsation with some dulness over the left back were also found in this patient; in the remainder all these signs were absent. Two patients showed indications of pulmonary compression, diminished breath sounds in one and bronchovesicular breathing in the other, but as both had large hearts it was difficult to be certain that the aneurysm was the sole cause of the signs. In three patients a diminished mobility of the left side of the thorax was noted, and in one of these a lessened excursion of the left side of the diaphragm was seen with the fluoroscope. In two patients there was sensitiveness of the dorsal spines, and in three a zone of disturbed sensation around the left side of the body.

The great value of *x*-ray examinations is apparent in such cases as these. One is often astounded to see the size of the aneurysm that has escaped detection by the ordinary methods of physical examination. The difficulties encountered in the interpretation of *x*-ray findings[9] are certainly negligible compared with the difficulties surrounding the use of ordinary methods of diagnosis.

As a result of our experience with aneurysms of the descending thoracic aorta we cannot do better than quote the words of Huchard when he speaks of aneurysmal neuralgias: "When one is dealing with symptoms of pain characterized by their persistency, their long duration, their intensity, when they remain unexplained, when they resist all ordinary medication, finally, when they present certain special characteristics, such as a fixed location or a diminished severity in certain attitudes of the patient, then we are not dealing with true neuralgia, as is too frequently assumed. In such cases one should consider aneurysm as a probable diagnosis, and if no tumor is perceptible as yet, one should turn to the *x*-rays in order to obtain certain proof."

[9] Sewall and Childs, The Interpretation of *X*-ray Pictures as an Aid to the Early Diagnosis of Thoracic Aneurysm, AMER. JOUR. MED. SCI., 1907, cxxxiv, 360.

THE REVERSION THEORY AND CLASSIFICATION OF GOITRE.

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I.

In making a daily study of goitre, grossly and microscopically, in the fresh and fixed condition, after examining specimens from 700 cases with their histories, and after reviewing the literature which recently has become extensive, I have been struck by the variance of the opinions and also the variance in the methods of attack in the study of the etiology.

The symptomatology seems, at least in well-developed cases, to be clearly known, and is well summarized in recent articles, such as those of Barker, Kocher, Halsted, Mayo, and others. I feel that there are early cases which are not diagnosticated as soon as they should be, because the symptoms are not associated with noticeable external glandular enlargement; it behooves the examining physician, therefore, to consider the possibility of hyperthyroidism in all cases of tachycardia and extreme nervousness. Such a diagnosis, however, does not mean surgical treatment always, although it is often in these early cases that complete recovery is seen following operation.

Briefly it may be stated that the etiology of hyperthyroidism is still far from being satisfactorily explained. Before beginning the study of goitre, we must first consider the normal biology of glands in general and of the normal thyroid.

If we review briefly the anatomy and function of the normal epithelial glands, such as the breast, salivary glands, and the pancreas or the liver, we find that all these start embryologically as invaginations, either of the endoderm or the ectoderm, and that the anatomical and the histological unit of these glands, with the exception of the liver, is an alveolus lined by one layer of epithelium, which hypertrophies and secretes into the alveolus. It may be further noticed that the secretion of each gland has one or more definite functions (nutritive, excretive, or protective) which are stimulated to activity either by the senses, sight, smell, taste, hearing, or touch, the sensations of which are transmitted through the nerves, or by some chemical substance[1] put into the circulation by some other cells in another

[1] See the work of Dolinsky (1895), who discovered that acids brought in contact with the mucous membrane of the duodenum set up promptly secretion of the pancreatic juice. This action was supposed to be reflexly through the nerves, but since the work of Popielski, Bayliss, and Starling, which shows that this action takes place after the nerves are severed, some other explanation has been thought of. They determined that if an extract of the mucosa of the duodenum and 0.4 per cent. HCl were made and injected into the blood, pancreatic secretion would be set up. The especial substance formed by this mixture they have called "secretin," and Starling has referred to it as a "messenger" from the duodenum through the blood to the pancreas. Howell's Text-book of Physiology, p. 703, and Bayliss and Starling, Journal of Physiology, 1902, xxviii, 325.

part of the body, or by both of these means. The epithelial glands which open into the alimentary tract either directly or by ducts, as do the buccal, salivary, gastric, intestinal, hepatic, and pancreatic, have one or more of the following functions; the production of a diluent, a mucilaginous material and ferments, or at least some digestive substance.

The thyroid is an epithelial gland conforming to the above anatomical conditions with the exception that it does not in its present condition possess a duct into the alimentary canal. We are, however, justified in believing that it probably did, at one time in the development of man, open into the canal by a duct, since most surgeons of extensive experience have operated on cysts of the thyroglossal duct, which has its origin in the gland and its opening in the foramen cæcum. Anatomically the thyroid is a well-defined gland, histologically not unlike some other epithelial glands, located near the alimentary canal, and showing at times remains of a duct emptying into it.

If such a gland emptied its contents into the alimentary tract, the contents probably had one or more of the above-mentioned functions of glands, as it is hardly conceivable from any known facts about any other glands similarly situated, that one so located would be without such a function. When, in the periods of man's phylogenetic history, he has been put under an environment which lacked the normal stimulus[2] necessary for the continuance of such an organ is not known. There was, however, a period in his racial development when this gland had a more extensive function.

This I believe to be a fair assumption from its anatomy and the facts known regarding the gradual disappearance or diminution in function of other organs, such as the loss of function in the male breast, diminution of the function of the toes, loss of body hair, and loss of function of the appendix. Other examples may be perhaps found in the economy of the organism.

With such facts and suppositions before us, and having some knowledge of the process of reversion, as seen in organs, in plant and animal life including man, especially the latter, in whom we see secreting male breasts, secreting supernumerary breasts, polymastia, bicornate uteri, etc., it is not unnatural to think of the possible partially rudimentary thyroid as reverting to its original activity.

In case this ductless gland should revert to a more extensive activity, what would occur in it? The first evidence would probably be hypertrophy and secretion. If this occurred, two things are possible: Either there would be a cyst formation, or absorption of the products produced. These two possibilities are often seen in other organs: for example, in the liver and kidneys under obstructive

[2] In calling this a normal stimulus, liberty is taken from a knowledge of the action of all the other epithelial glands in the human body as it exists now. These glands are stimulated to activity normally by certain substances under certain conditions.

conditions. In the liver the backing up of the secretion causes dilatation of the ducts, enlargement of the liver, but seldom cyst formation. The secretion under such pressure is supposed to get into the lymphatics and thus into the circulation, giving evidence of this in jaundice and toxemia.

In the kidney a similar process is seen, with perhaps a greater tendency to the production of cysts. However, here, too, we see both conditions in which there is also re-absorption of the products of secretion and resulting toxemia. Why the cyst formation should occur in one instance and not in another is not known.

These processes in the kidney and liver and other glands are very similar to those seen in the "simple cystic" goitre and the "exophthalmic" goitre. In the former case the alveoli are markedly distended and contain products, the pressure of which flatten the epithelial lining and in some cases produce complete atrophy of the cells, so that the whole thyroid exists as a foreign body composed of cysts and only causing inconvenience by pressure. When, however, there is complete atrophy of the secreting surface a condition of myxœdema may occur, as we shall see later. Early in the case of "exophthalmic" goitre the material secreted is not stored in the alveoli, but is re-absorbed, and it is in these cases especially that the toxemia is seen, although toxemia does occur, as we shall see later, in some cystic goitres under certain conditions (Fig. 5 *a* and *b*).

Like the absorbed products of the kidney and the liver, the products of the thyroid produce toxic symptoms and even death, with the changes seen at autopsy which occur in other toxemias. The liver is fatty, there may be changes in the kidneys, the heart is often fatty and markedly dilated.

The clinical picture is one of toxemia with mental, nervous, and digestive disturbances. The substance or substances which produce this toxemia are the products of the thyroid, since their associated iodine has been demonstrated in the blood of patients suffering from hyperthyroidism. Similar symptoms can be produced experimentally by the overfeeding of the products of the thyroid. Removal of the greater portion of the secreting gland reduces the symptoms and often causes them completely to disappear. We must, therefore, consider the toxin, so to speak, as being the product of the gland itself, just as the toxic substances in the cases of the kidney and liver are products of their own secretion.

In the case of the thyroid, however, a certain amount of the secretion is apparently necessary for the well-being of the individual, because we see death following total extirpation of the gland. These cases go on to a condition of myxœdema which can be relieved by feeding the products of the gland.

In the condition of cretinism, in which there is an absence of thyroid secretion and a concomitant physical underdevelopment, great improvement may be seen after thyroid feeding. All of these

examples seem to demonstrate the possible physiological necessary of the products of the thyroid. The contrast between a patient with hyperthyroidism and one with hypothyroidism is very marked, the conditions being clinically quite opposite, in that one is the subject of extreme activity, while the other is the subject of extreme apathy or sluggishness. The necessity of the thyroid for the economic equilibrium has two possibilities for its solution. Either the products normally secreted are re-absorbed, or there is an "internal" secretion. The whole problem of internal secretion is one about which we are not so absolutely certain, unless we give it a very broad meaning in that each organ really contributes something to the body fluids which is characteristic of itself. This is perhaps a correct one in view of the results obtained from the studies of immunity. It must not be forgotten that the internal secretion may be twofold, as that in the liver in which one product is for nutrition (glycogen) and the other for elimination (urea).

It may be stated that at present we are beginning to look upon the different types of goitre as stages in one general process. This is seen histologically in the type known as "exophthalmic goitre" (Fig. 4), which histologically is an exaggerated picture of the process of papillary projection formation (Fig. 5 *b*) found in some of our "colloid" goitres, which give "exophthalmic" symptoms. This is so true that in the routine examination of sections from different areas I have, for want of any definite name, in some cases written my report "colloid goitre with exophthalmic areas," or "colloid, fœtal, and exophthalmic goitre," recognizing in these specimens all three types well developed. At times it is possible to demonstrate areas which are absolutely typical "exophthalmic goitre," and in other areas find typical fœtal adenoma and typical "colloid" goitre. These findings have led Dr. Wilson and me to believe that the so-called "types of goitre" are not "types" but "stages." Why one thyroid should develop into a cystic or "colloid" goitre and another into an "exophthalmic" goitre is unknown, just as the process of cyst formation and its counterpart, the absorption without cyst formation, in the kidney and liver are unknown.

In view of the fact that the thyroid is an epithelial gland, producing a secretion which seems necessary for the body economy, and that this secretion was most probably emptied into the alimentary canal through a duct, the question of the normal stimulation of this activity naturally presents itself, since we know that all the other epithelial glands act as a result of some type of physiological stimulus.

The question arises: What was the normal stimulus for the thyroid under its original conditions, and would the same thing stimulate it again to activity under a condition of reversion, as we see it in the supernumerary breasts? I have recently had a case of a woman, who was brought to the clinic with a diagnosis of lipomas in the axillæ, which when removed proved to be functionating supernumerary

breasts without ducts, there being absolutely no sign of nipples. These tumors appeared at puberty and had recently become markedly hypertrophied during pregnancy. We have in this case breasts which are rudimentary and ductless, stimulated to activity by the natural stimulus for the natural breast activity. The patient was otherwise normal. The breasts upon microscopic examination presented the picture of normal breasts with the exception that the acini were markedly dilated or cystic, and contained a somewhat thickened milk. The interglandular tissue, especially that immediately surrounding the alveoli, was infiltrated with lymphocytes.[3] It is these facts and the analogy of the thyroid to other glands and their activities which led me to the reversion hypothesis for the condition known as goitre, without attempting to state the real etiological stimulus.

May the process known as goitre be expressed as an attempted reversion of the thyroid to its original function, being stimulated to activity by the same substance which stimulated it to activity in primitive man? What this stimulating substance is, where it is found, and how it stimulates the gland to activity is unknown.[4] Whether this factor is organic or inorganic, living or dead, is left to the etiologists. In presenting such a theory it seems to me that it may stimulate further investigation, not only among medical men, but among biologists generally.

The physiological chemist has a great field before him in determining the source in the intestinal contents, either as a substance taken into the tract or as a result of breaking down or synthesis of organic or inorganic substances. He may also busy himself with the products of metabolism found in the fluids of the body which may contain the substance or living thing which causes the hypersecretion of the organ. Perhaps such an hypothesis may open a new field of research; it is with this view that I have taken the liberty of publicly expressing it.

[3] Often associated with the process of absorption is seen a round-cell infiltration. This condition in goitre has led many to conceive of an etiological process of an infectious nature. This round-cell infiltration has been found in thyroids of individuals who have given no history of having any symptoms of hyperthyroidism or enlargement of the gland, although I may suggest that perhaps a great many individuals undergo some symptoms of hyperthyroidism unnoticed and perhaps unrecognizable in the thyroid microscopically.

[4] The stimulation of glandular activity, while it is not clear in most cases, shows itself dependent upon normal conditions. The mammary glands, for example, are stimulated to hypertrophy and secretion during pregnancy by some influence started in the female pelvic viscera. What this is or how it acts is unknown. The glands of the stomach are stimulated to activity by the sensation of eating (psychical), by stimuli in the mouth and nostrils. It seems (Howell's Text-book of Physiology) that some foods contain substances capable of effecting the secretion, and that "meat extracts, meat juices, soups, etc., are particularly effective in this respect." Howell says that "certain common articles of food, such as bread and white of eggs, have no effect of this kind at all." He speaks of the "mechanism of secretion," and divides it into groups: (1) The psychical secretion. (2) The secretion from secretagogues contained in the food. (3) The secretion from secretagogues contained in the products of digestion. He makes the statement that the chemical nature of these last named stimuli is undetermined. One may clearly say that all glands in the human body are stimulated to activity by something which has to do with the body economy.

II.

In classifying and recording my observations on the material in Drs. Mayo's clinics I have found the following scheme of value, not only to the pathologist but especially to the clinician. For their

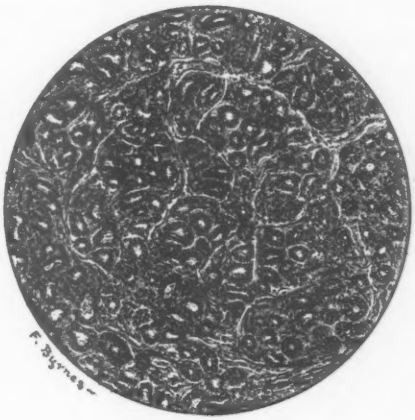

FIG. 1.—Fœtal thyroid.

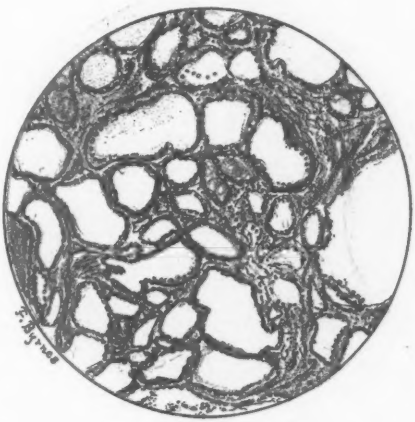

FIG. 2.—"Normal" thyroid.

convenience I have tried to state the conditions, "types" of normal thyroid and goitre, as we know them. The following classification has been adopted as the simplest, and represents the histological types or stages of goitre, from which the clinical picture may be deducted.

The fœtal thyroid (Figs. 1 and 7*a*) contains no histological visible secretion so far as we know, and yet it is the forerunner of some of our goitres (fœtal adenomas) (Fig. 6) which retain the fœtal type. Diagramatically it may be represented in Fig. 7*a*). The "normal" thyroid (Figs. 2 and 7*b*) is composed of alveoli lined by one layer of

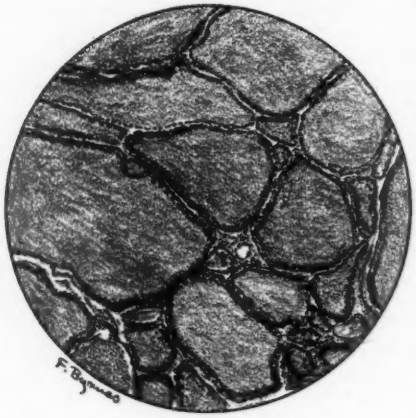

FIG. 3.—Cystic thyroid.

FIG. 4.—Hypertrophic parenchymatous goitre.

epithelium; it secretes some substance, and contains a probably partially non-absorbable substance known as colloid, some of which at least remains in the alveoli. In the "simple goitre," or cystic goitre (Figs. 3 and 7*c*), in which the alveoli are large and filled with colloid, there is an excess of secretion and production of colloid

without an equal amount of absorption, and the condition may be represented by Fig. 7*c*. This type corresponds to the cystic kidney which gives no symptoms, but is still functionating, and is compatible with the life of the individual. In the type known as "exophthal-

FIG. 5 *a*.—Cystic goitre.

FIG. 5 *b*.—Papillary cystic goitre.

mic goitre" (Figs. 4, 7*d*, and 7*e*) there is an excess of secretion and increased absorption, with slight if any increase in colloid production. This type corresponds to the condition in the kidney and liver in which there is absorption without cyst formation or partial cyst formation.

There may also be a stage in which the symptoms are very exces-

sive, and in which, histologically, an extreme cytolysis is seen. We, therefore, have a condition of extreme excess of the products of the degenerating cells with increased absorption which, however, may not necessarily be equal to the amount of secretion. This may occur

FIG. 6.—Fœtal adenoma of the thyroid.

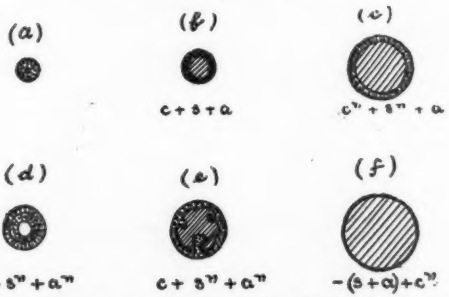

FIG. 7.—Diagrammatic representation of *a*, the fœtal thyroid; *b*, normal thyroid; *c*, cystic goitre; *d*, hypertrophic parenchymatous goitre; *e*, papillary cystic goitre; and *f*, the cured type of cystic goitre. In the algebraic representation of the conditions, *c*, equals colloid production; *s*, absorbable secretion, and *a*, the process of absorption. Any of these may be increased in the conditions, and this is represented by raising the letter to the *n*th power.

in the papillary cystic (Fig. 5 *b*), hypertrophic parenchymatous (Fig. 4), and fœtal adenoma (Fig. 6).

There is still another stage, which may be termed the cured stage (Fig. 7*f*); cases which have withstood the overgrowth and excess of secretion and cytolysis until there remains a large tumor composed of alveoli, lined by thin connective-tissue or atrophic cells instead of healthy epithelium, and filled with colloid material. These patients suffer only the inconvenience of a tumor without the toxic effect.

True enough, however, some of these go on to myxœdema as a result of the lack of secreting surface. This condition is really a minus condition, or a condition of hypothyroidism (Fig. 7 *f*). It may be well compared to the hydronephrotic or cystic kidney, which has little or no functionating surface. These types or stages are those which we recognize both histologically and clinically.

If we assume that the thyroid has a more extensive function in primitive man than it has at present, and we are from analogy perhaps justified in making this assumption, we must endeavor to express the condition in primitive man.

First, however, the human organism today contains a "normal" thyroid which represents colloid production, an absorbable secretion, the process of absorption, and no excretion into the alimentary canal. The welfare of the organism is dependent upon its food supply, the process of digestion, and air, and would live advantageously if it were not for the entrance of antagonistic organisms or substances through the portals of entry, the substances which arise in the intestine, or as a result of metabolism. Normal man and his relations to his thryoid may be expressed by saying that he has air, food products (including water), the process of digestion, and a glandular organ (thyroid), which produces colloid material, an absorbable secretion, and shows the process of absorption, but does not empty its secretion into the alimentary canal.

Primitive man had air, food products (including water), the process of digestion, and a glandular organ (thyroid) which produced a secretion which was excreted into the alimentary canal, because we assume that his relations to the thyroid were only different from the present relations in that the thyroid had a more extensive function and emptied its secretion through the thyroglossal duct into the alimentary canal, where it probably had some function which does not exist as such, at least to the same extent, in present-day man.

From a knowledge of the process of secretion in other glands based upon experimental evidence, such as the experiments upon the duodenum with hydrochloric acid which produces some substance which gets into the circulation and thus stimulates the pancreatic and hepatic secretion, and the process of secretion in the breasts as stimulated by the developing fœtus in utero, and perhaps also the increased secretions of the salivary glands, which may have some chemical stimulus, I have been led to consider a somewhat similar process in connection with the original normal activity and the abnormal activity of the thyroid gland. What the stimulating thing is, living or dead, organic or inorganic, is at present not known. The possibilities may be briefly stated as follows: (1) The stimulating something may be in the food products (including water); (2) it may be in the products of metabolism; (3) it may be in the air which the individual breathes; and (4) in accordance with the hypothesis of this paper the unknown stimulating substance is supposed to be

the unknown substance which stimulated the gland to activity in primitive man, it acting in cases of goitre upon a rudimentary gland.

Without regard to the etiological factor or the nature of the process in goitre, but for the use of the pathologist and clinician, the material which I have studied may be grouped under simple convenient headings. The terms "exophthalmic" goitre, "colloid" goitre, and "simple" goitre, etc., have no very definite histological meaning, nor have they any definite clinical meaning as we now understand the conditions. We, therefore, should attempt a classification based upon pathological findings in exophthalmic goitre which have been well worked out by my colleague, Dr. Wilson, and the other types as worked out from my observations.

The "simple" goitre or "colloid" goitre which we recognize clinically as an enlargement of the thyroid without symptoms other than pressure, should properly be called a cystic thyroid or cystic goitre (thyroidea cystica) (Figs. 3 and 7*c*), because the tumor histologically is composed of multiple small or large cysts with their contents. The term "exophthalmic goitre" is based upon one clinical sign, exophthalmos, which is not constant in cases of hyperthyroidism. On the other hand, there are cystic goitres which sometimes show exophthalmos, and hyperthyroidism with or without exophthalmos.

There are two conditions connected with the "exophthalmic goitre," as it has heretofore been generally although not commonly understood, which seem positive. One is the histological picture of increase in the epithelial or secreting surface of the gland, and the other, the clinical condition, hyperthyroidism. Histologically, therefore, this stage may be termed hypertrophic parenchymatous goitre or thyroid (thyroidea parenchymatosa hypertrophica) (Figs. 4 and 7*d*). There is little or no cyst formation, but only a hypertrophy of the parenchyma.

A third type or stage is clinically and histologically the cystic goitre, which at some period develops symptoms of hyperthyroidism and which histologically shows the cysts filled with colloid material as in the cystic goitre, with the addition that there are papillary projections into the lumina of the alveoli with consequent increased secreting surface, therefore, approaching the hypertrophic parenchymatous goitre histologically and clinically. This type may be the papillary cystic goitre or thyroid (thyroidea cystica papillare) (Figs. 5*a* and *b*, and 7*e*).

A fourth type or stage is that one seen histologically as a hypertrophic fœtal thyroid in which there is a small amount of epithelial tissue and a great amount of interglandular connective tissue. Clinically, this type is the goitre of the cretin with tumor formation and hypothyroidism. We shall call this condition hypertrophic fœtal thyroid (thyroidea fœtalis hypertrophica).

A fifth type and a more common type than the last one is the fœtal adenoma or adenomatous hypertrophy of fœtal thyroid instead of the

connective-tissue hypertrophy seen in the last type. This type clinically is seen usually as a tumor which may or may not cause any other inconvenience than that of pressure. It usually is an encapsulated tumor in the thyroid, and can be shelled out. However, when the encysted or encapsulated fœtal adenomas occur, the tissue may degenerate from some unknown reason, or perhaps from circulatory changes due to the thickened capsule, and then the products may be rapidly taken up by the lymphatics and thrown into the circulation, giving symptoms of hyperthyroidism. This type may be termed fœtal adenoma of the thyroid (thyroidea fœtalis adenoma tosa) (Figs. 6 and 7 *a*).

RESUME. 1. The process of goitre may be a process of reversion of the thyroid gland to some former function.

2. Hyperthyroidism is a toxemia the result of absorption of the products of the hyperactive thyroid.

3. The stimulus causing the hyperactivity may be the same that stimulated the thyroid to activity in primitive man.

4. This stimulus was then probably a normal stimulus to the gland, just as we have normal stimuli for glandular activity in man in his present condition.

5. This stimulus may still be present in the food or water, formed through some process in the intestine or in the metabolism of the body, or it may exist in the air.

6. The types of goitre are probably not types but stages in a general process.

7. Goitre may be classified upon a pathological basis as follows: (*a*) Cystic goitre (thyroidea cystica) (Fig. 3). (*b*) Hypertrophic parenchymatous goitre (thyroidea parenchymatosa hypertrophica) (Fig. 4). (*c*) Papillary cystic goitre (thyroidea cystica papillare) (Fig. 5 *a* and *b*). (*d*) Hypertrophic fœtal thyroid (thyroidea fœtalis hypertrophica). (*e*) Fœtal adenoma of the thyroid (thyroidea fœtalis adenomatosa) (Fig. 6).

8. Hyperthyroidism always occurs in *b* and *c*, and may occur in *e* (Figs. 4, 5, and 6).

THE NATURE, DIAGNOSIS, AND TREATMENT OF METABOLIC OSTEO-ARTHRITIS.

SO-CALLED RHEUMATOID ARTHRITIS, ARTHRITIS DEFORMANS, ETC.

BY P. WILLIAM NATHAN, M.D.
OF NEW YORK.

IN a series of papers on the classification of the joint diseases generally known as rheumatoid arthritis, arthritis deformans, etc., published in this journal,[1] this supposed group of joint diseases was shown to be composed of a number of dissimilar diseases. It was

[1] January, April, December, 1906.

further shown that the joint diseases generally, and with them the so-called rheumatoid affections, like the diseases of other organs, could be divided into two fundamental classes—the inflammations (infections), and the degenerations (trophic diseases). Moreover, it was shown that the joint diseases could be further subdivided, according to the original location of the disease, into synovial forms (arthritis) and osseous forms (osteo-arthritis), so that by the use of four simple and definite names we could indicate a definite clinical entity corresponding to definite pathological changes, without having recourse to a long description of the malady in order to make our meaning clear to others.

Thus, there is: (1) Infectious arthritis, an infectious joint disease involving the soft parts primarily; (2) infectious osteo-arthritis, an infection involving the bones primarily; (3) trophic arthritis, a degenerative joint disease involving the synovia only; and (4) trophic osteo-arthritis, one involving both the bones and soft parts. These names, it was shown, could be made still more definite when the etiology is known; so, for instance, pneumococcic osteo-arthritis, a pneumococcic infection involving the osseous structure of the joints, having the general characters of infectious osteo-arthritis; or neurotic osteo-arthritis, a trophic degenerative change involving the osseous joint structures due to nerve lesion—as in tabes, syringomyelitis, etc. In the last paper of the series it was shown that by means of this classification the so-called rheumatoid conditions could be differentiated from one another clinically.

However, as these papers were simply preliminary, giving only a general view of the subject, many details of the pathology, etiology, and the symptoms of the various diseases were purposely omitted in order to simplify the subject. This was particularly the case with the disease designated as metabolic osteo-arthritis and corresponding to Schuchardt's arthritis nodosa, Baumler's arthritis deformans, and Goldthwait's atrophic arthritis, of which only a few leading features were discussed. As this disease presents many interesting features which are still misunderstood, or the subject of controversy, and, as I believe, the results of my investigations are definite enough to give us a more intelligent conception of the disease, I purpose to deal with this subject, in detail, in the present communication.

In studying a disease of an organ the first point to be decided is, Is it a local condition, causing secondary general symptoms, or is the disease a part of some general condition, that is, is the disease primary or secondary? If the disease of the organ is primary, the study of the pathology and symptomatology as they refer to the organ may lead to a better understanding of the etiology and pathogenesis of the disease. When, however, the disease of the organ is secondary or a part of some general morbid process, the study of the local condition can, of course, never lead to a true conception of the disease itself.

Though the majority of observers have looked upon metabolic osteo-arthritis as a joint disease caused by some uniform general abnormality, the search for the cause and pathogenesis has nearly always been confined to the joints only. It is true that for many years a general metabolic abnormality (excess of uric acid) has been considered the cause of the joint disease and of the general condition; but since it has been shown[2] that uric acid has nothing to do with the disease, only the local condition has been considered. If, as has been assumed, metabolic osteo-arthritis is a general disease, it is futile to expect to discover the pathogenesis or cause by studying the joint condition only. The most we could hope for would be a better understanding of the local condition. But not even the joint condition has been carefully studied. The descriptions of the symptoms and course of the disease to be found in the general literature are either inadequate or inaccurate; and the pathology, studied in subjects (dead of some intercurrent malady) without a history of the joint disease, or by means of museum specimens without any clinical data whatsoever, is seriously misconceived. In the present instance it is, therefore, necessary to arrive at a definite understanding of the local condition, before we can discuss its relation to the general manifestations of the disease or of the disease itself. Hence, the study of the subject is divided into the following parts:

1. The study of the joint conditions: (*a*) to establish a clinical entity; (*b*) the diagnosis of the joint condition, that is, its differentiation from all other joint diseases.

2. The pathology of the joint disease. Not the pathology of a general disease is intended, but only the anatomical findings in the joints of individuals who have presented, during life, the joint condition herein described.

3. Having established a definite joint condition with definite and easily recognizable anatomical changes, the general symptoms presented by individuals with such a joint abnormality will be discussed.

4. From the study of the joint symptoms and the general symptoms, I shall attempt to decide whether the disease is primarily a joint disease causing general symptoms or a general disease with joint involvement.

5. Granting the disease is general, the question then to be decided is, the nature of the general condition. Is it a definite and specific abnormality, or might not, as is so often the case with other joint diseases, a number of dissimilar general conditions be instrumental in its production.

6. These points having been more or less satisfactorily settled, a method of treatment which in my hands has been of benefit, will be detailed.

[2] McCrudden, Uric Acid, Boston, 1905.

THE JOINT SYMPTOMS. *Muscular Atrophy.* Muscular atrophy is always a very early symptom of joint disease, and not infrequently can be detected before the other physical signs of joint disease present themselves. In no other joint affection, however, does it appear so early, or is it so marked as in metabolic osteo-arthritis. Not only does it appear early, but it progresses more rapidly and quite out of proportion to the other joint manifestations. At times it becomes extreme; and when the disease attacks the joints of the hands and fingers, which is usually the case, the condition might be mistaken for one of paralysis. Indeed, when flexion deformity predominates, the hands may exactly resemble the paralytic claw hand (Fig. 1). Though the muscular atrophy is not always so intense, it is very

FIG. 1.—Pure flexion deformity in metabolic osteo-arthritis in a girl aged ten years. There is no swelling; the hand resembles the paralytic claw hand. The disease had existed for four years.

marked in the majority of cases; and whatever may be its cause in other joint diseases, it seems to me quite improbable that this extreme atrophy, which is present so early and whilst the limb is still in condition to perform at least some of its functions, should be due to the joint disease alone.

Subjective Symptoms. The earliest symptom complained of by the patient is joint stiffness. This is much more pronounced when the disease begins in the hands, and especially so in those engaged in pursuits which require fine manual adjustments. The stiffness is said to be more severe upon arising in the morning, and gradually disappears to a certain extent during the day. As time goes on, however, it extends over longer and longer periods, and finally becomes constant. If the joints are examined during this time,

before joint swelling and the signs of actual joint irritation have made their appearance, it will be found that passive motion is hardly, if at all, limited, though the patient complains of the stiffness. It, therefore, seems more probable that what the patient calls stiffness is really weakness. Indeed, the more intelligent patients do not complain of stiffness, but of gradually increasing weakness. With the weakness various other subjective symptoms are present. Patients complain of formication, etc., and pain.

Pain. Pain is a most variable symptom. It not only varies in the different individuals, but in the different joints of the same individual. In some joints the disease runs its course with slight or no pain at all; in some it is severe but transitory; in others it is intense, constant night and day, and unaffected by immobilization for weeks or months. The character of the pain is similarly variable; it may be dull or sharp and lancinating, and may or may not be increased by passive motion. When present it is always increased by pressure upon the bone near the joint.

As all these patients are chronic invalids and many of them present decided signs of functional nervous derangement, I have often been unable to decide whether or not the pain is due to nervous influences. In some cases I indeed suspected an hysterical element; but in the majority of them the long-continued sleepless nights and the total failure of suggestive treatment (hypodermic injections of water, etc.) have convinced me that the pain is real and not imaginary; the more so as I have known it to be very intense in patients with absolutely no neurotic symptoms. In one case (a lady, aged thirty-five years), with all the joints involved except the spine and maxillæ, the pain in the ankles continued intense for a number of weeks, and nothing relieved her but opium given in suppositories. After the pain ceased the patient discontinued the suppositories voluntarily.

So far as I can make out, the pain does not correspond to any particular stage of the disease. It is usually present early, and in the majority of cases is most severe when the disease is most active. It usually subsides with the subsidence of the joint destruction, but it may be mild in the earlier stages and very severe later on. In certain forms of the disease in children there is practically no pain at all.

Joint Swelling. The peculiar form of swelling which occurs in metabolic osteo-arthritis has been considered by the earlier English and French writers the most characteristic symptom of the disease. Because of it, Heygarth named the condition nodosity of joints; Trousseau called it rheumatisme noueux; and still more recently Schuchardt called it arthritis nodosa. There can be no question that the peculiar nodular swelling is a very characteristic symptom; but the swelling is not always nodular; if present at all, it is only present for a limited time; and it may be masked by joint effusion.

Weakness or stiffness, pain, and other subjective symptoms pre-

cede the joint swelling by a variable length of time. This interval depends upon two factors: (1) The rapidity of the progress made by the disease; (2) the external mechanical conditions. In some cases atrophy and weakness progress rapidly; the affected extremities are painful and soon become so weak that active function is impossible. In these, when the disease attacks the upper extremity, it runs its course uncomplicated by mechanical joint irritation, and the characteristic joint swelling soon makes its appearance. In others the weakness is very slowly progressive, and in those whose occupation does not entail the constant use of the affected parts, the preliminary joint symptoms may exist for some time

FIG. 2.—The hands in a very early stage of metabolic osteo-arthritis. There is no effusion, but a very slight spindle-form swelling. The fingers are just beginning to deviate laterally.

before joint swelling. On the other hand, in those who use the extremities constantly or violently the joint swelling soon makes its appearance whether the disease progresses rapidly or not.

Not only is the period before the advent of joint swelling variable in correspondence with the internal and external conditions, but the character of the swelling depends upon them. Thus, in those cases with severe, rapid progress and early cessation of function, it comes on gradually, is at first spindle shaped (Fig. 2), and later, due to a thickening of the soft parts, assumes the characteristic nodular form (Figs. 3 and 4). When the disease progresses more gradually and more slowly and the early subjective symptoms are milder, it permits of more or less active function for a longer period. In such cases, the joints perform their functions under abnormal conditions, and, as a

FIG. 3.—Symmetrical and general nodular swelling in a case of metabolic osteo-arthritis. The glands and spleen are enlarged and palpable. So-called Still's disease.

FIG. 4.—Nodular swelling of the hand and finger-joints in metabolic osteo-arthritis. In this case all the joints except those of the head and neck were involved. The liver, spleen, and glands were enlarged (Fig. 15).

consequence, the symptoms of joint irritation usher in the disease. The swelling then appears abruptly, is irregular or spindle-shaped, and, besides thickening of the soft parts, there is joint effusion. In this event, with the appearance of the swelling, there is loss of motion, pain, and deformity (in the hands the appearance is illustrated in Fig. 5). For this reason the joints are put at rest and the effusion then subsides to a certain extent, leaving the doughy spindle-shaped or nodular swelling behind. In the more energetic or in those who are compelled to work, depending upon the rapidity of the advance of the disease, this sequence may be repeated a number of times. It must, however, be remembered that the effusion is often very slowly absorbed, and in a fair number of cases remains permanently.

FIG. 5.—Flexion deformity with reactive effusion in metabolic osteo-arthritis. The effusion in this case almost completely disappeared when the joints were put at rest.

As joint effusion may occur from joint irritation, irrespective of the cause, it cannot, of course, be considered a characteristic symptom of any form of joint disease. Nor is nodular swelling an absolutely pathognomonic symptom of metabolic osteo-arthritis. In children it frequently involves all the joints of the extremities and remains present throughout the course of the disease (Fig. 2). But in adults, though it is nearly always present in the knees, it rarely involves the smaller joints of hands and toes. Moreover, certain forms of poly-articular infection with para-articular involvement which occur in children are characterized by a doughy nodular swelling of the joints. Such cases have frequently been mistaken for metabolic osteo-arthritis or have been considered analogous to it (rheumatoid arthritis,

arthritis deformans); and when, as sometimes happens, there are swollen glands, they have been described as Still's disease. This will be more fully dealt with later.

Joint Deformity. With the advent of the swelling, or soon after, muscular contraction, and with it joint deformity, makes its appearance. To the deformity the disease owes one of its most popular names. Virchow, I believe, first named it arthritis deformans. Following him, a great many Germans, and more recently some English writers (Garrod), call it so. Charcot, whilst he did not adopt the name, also considered the deformity one, if not the most, characteristic part of the condition. Indeed, he went so far as to divide the cases into types, according to the various forms of deformity which occur in the hands.

FIG. 6.—Palisade deformity in metabolic osteo-arthritis. There is no swelling.

The most characteristic deformities occur in the fingers. They are the so-called palisade deformity: flexion of the middle and extension of the terminal phalangeal joints (Fig. 6); deviation of the fingers to one side (Fig. 7); and flexion of the phalangeal, and phalangeal metacarpal joints (Fig. 1). Various forms of deformation may exist in the same patients in different joints, and combinations of any or all of them occur. In the larger joints the deformity differs in no wise from that which occurs in all other forms of joint disease. The knee is flexed and perhaps adducted; in the hip flexion and abduction are later succeeded by adduction and internal rotation.

Here, as in other joint diseases, the deformity depends upon two factors, viz., muscular contraction and tissue destruction. In the early stages deformity is due to muscular contraction alone, in the later stages to a combination of muscular contraction and bone destruction. In no other condition is this so well exemplified as in metabolic osteo-arthritis. In this condition, as well be shown later,

rarefaction and softening of the articular ends of the bones precedes or is concomitant with the earliest joint symptoms. The softened bone not only gives way as the result of the pressure of muscular contraction and weight bearing, but later the location of the softening and absorption directly influences the extent and direction of the deformity. In the terminal stages of the disease, the articular ends of the smaller bones (fingers and toes) are more or less completely absorbed, and to this is due the striking deformity of the fingers. By means of a series of *x*-ray pictures the gradual evolution of the deformity may be graphically depicted.

Loss of Motion. Loss of motion depends upon a number of contingencies. In the early stages, as has been said, weakness is apt to be mistaken for stiffness, but later, when there is swelling and mus-

FIG. 7.—Lateral deviation of the fingers without swelling in metabolic osteo-arthritis.

cular contraction, there is, of course, real limitation of motion. In those cases in which the swelling remains nodular, contraction may be slight or transitory or entirely absent and passive motion may not be interfered with to any great extent. When muscular contraction is present, which sooner or later is the case, passive motion, unless there is mechanical joint irritation, is limited to the extent of the contraction, and the joint is quite freely movable within the limits of the contraction. So, for example, flexor contraction of the knee limits the motion in extension, but the knee may be still further flexed without difficulty. When, however, the contraction has existed indefinitely, and the joints are retained in one position for a long time, there is apt to be some further limitation of motion. Except during the transitory periods of joint irritation the limitation of

motion is never absolute, nor does it keep pace with the progress of the disease; for patients with extensive disease and much deformity often have a considerable range of passive motion.

Though some of the joint symptoms are peculiar and often very characteristic, it is evident that in metabolic osteo-arthritis, just as in other joint diseases, it is harzardous or impossible to make a positive diagnosis upon the intrinsic joint symptoms alone. Owing to their superficial situation and their peculiar functions (motion and weight bearing), the joints themselves present essentially the same intrinsic symptoms in all forms of disease. Thus, pain, swelling, muscular spasm with its attendant deformity, and loss of passive or active motion appear as symptoms of not only all forms of joint disease, but, indeed, may be induced by joint irritation caused by an abnormality near, but not directly involving the joint at all.

Hence, though advanced cases of metabolic osteo-arthritis present such a peculiar and characteristic deformation of the fingers that the diagnosis can be made from it without any difficulty, these symptoms are not so definite in the other joints and are not present at all in the early stages of the disease. Nodular swelling, characteristic as it is, is not pathognomonic; for such a swelling may appear in any condition with peri-articular infiltration and thickening. Pain is all extremely variable symptom. Muscular contraction is present in an joint diseases and deformity is dependent altogether upon mechanical conditions. We are here, as elsewhere, therefore, compelled to depend upon the influence which the character of the morbid process exerts upon the onset, course, and termination of the joint condition and upon the actual condition in the joint as shown by the radiograph, for the diagnosis. In metabolic osteo-arthritis this influence is definite and characteristic.

Onset and Course. The condition is always polyarticular and symmetrical. It always attacks the peripheral joints first and a number of joints are usually affected simultaneously. The onset is invariably insidious. There is no foundation for the division into acute, subacute, and chronic cases, advocated by Garrod. This classification, which is based upon the abrupt onset of the swelling, has led to the confusion of this joint condition with certain forms of polyarticular infection with which it has absolutely no connection. The abrupt onset of the joint swelling is due, as has been already explained, to mechanical irritation, and careful (not suggestive) inquiry will always elicit symptoms which have preceded the swelling. In a large percentage of the cases the disease comes on so insidiously that the patient is unable to state definitely just when the trouble began.

Not only is the onset insidious, but in cases uncomplicated by joint irritation the course is gradually progressive. In some cases, it is true, the disease progresses more rapidly than in others, but even in the most rapidly destructive forms the disease advances gradually,

and there is never a really abrupt onset and acute local and general reaction. In the majority of cases the disease progresses slowly and very gradually. Preceded by more or less decided subjective symptoms, a number of joints become weak or stiff. With increasing weakness or stiffness joint swelling appears; hardly perceptible at first, when uncomplicated by mechanical joint irritation, it gradually increases, becomes spindle-shaped, and then perhaps nodular. In many cases the nodular appearance of the swelling is due to the extreme atrophy of the peri-articular structures and not to thickening of the joint membranes or bones. Thus it remains for a variable length of time, when it just as gradually recedes, finally disappears altogether, leaving the joints atrophied and deformed. The deformity, in its turn, increases by degrees, and though passive motion may not be markedly limited, it gradually and progressively leads to crippling. In the meantime new joints become involved in the same insidious and progressive manner, and in the severer cases, beginning in the periphery and proceeding toward the trunk, all the joints, including those of the spine, may become involved. Though there are never intermissions, even in severe cases, there are times when the disease progresses less rapidly or remains stationary for a variable length of time. The periods of apparent quiescence may, indeed, continue for several years; but in the severer forms the condition ultimately resumes its relentless course and the individual finally becomes a helpless cripple.

In the milder cases the disease progresses very slowly, with long periods of quiescence and less extensive crippling. In some cases, indeed, the disease, after progressing to a certain extent, seems to remain stationary, and though the affected joints remain crippled, no more joints become involved. It is, however, very difficult to say definitely that the disease will make no further progress in a given instance; for it not infrequently again becomes active and progressive after years of quiescence.

Differential Diagnosis. With one exception (polyarticular form of senile osteo-arthritis, Heberden's nodes) there is no other chronic polyarticular joint condition in which the joints are symmetrically and progressively involved. In children the condition, because of the absence of joint irritation (they are not compelled to use the joints in spite of pain and disability, as adults often are), occurs in its purest form. In them the nodular swelling, which comes on very gradually, remaining present for a very long time, with slight or no loss of passive motion, is so characteristic that it is quite impossible to mistake it for any other joint abnormality. In adults, however, the inexperienced observer may occasionally find difficulty in making the diagnosis. This is most apt to be the case when the disease comes on very insidiously and progresses very gradually. In such cases the prodromal symptoms, being slight, may be overlooked and the frequently recurring symptoms of joint irritation might lead one to

believe there are recurrent attacks with an abrupt onset. Under these circumstances the slight rise in temperature which is occasionally present has led many otherwise good observers to believe that the malady is infectious. But if it is remembered that the polyarticular joint infections are always due to a general infection (sepsis), that the onset is very acute, with marked constitutional symptoms and rapid but not progressive joint involvement, this mistake in the diagnosis is readily avoided. What has caused most confusion in regard to the differentiation of these conditions are the cases of infectious polyarticular joint disease seen long after the initial disease

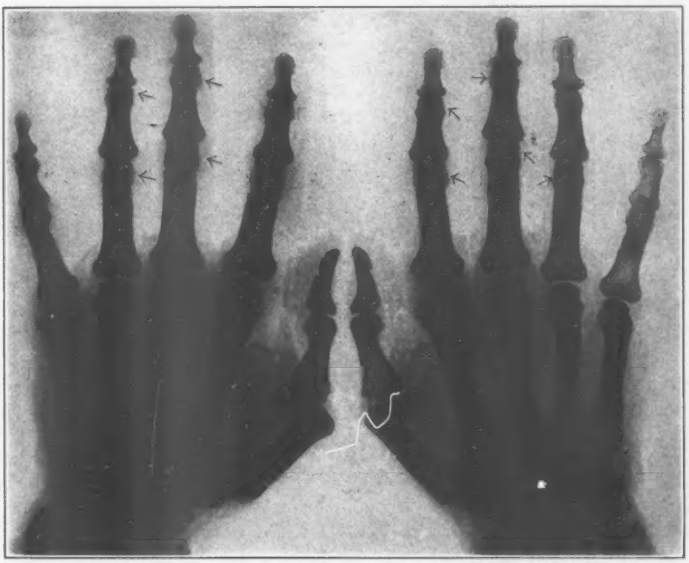

FIG. 8.—Radiogram showing the condition of the bones in a very early stage of metabolic osteo-arthritis. This picture is taken from a radiogram of the hands shown in Fig. 2. The arrows point to the rarefied areas. (Radiograms to show these changes must be properly exposed and developed very carefully.)

has subsided. In these, if the history is not obtained, the deformed and stiff joints of the hands may lead the surgeon to believe he has a chronic joint disease to deal with. Indeed, these cases are nearly always mistaken for cases of metabolic osteo-arthritis, and called rheumatoid arthritis, or arthritis deformans. This is unfortunate, for in cases of polyarticular infections we are not dealing with an active joint disease at all, after the acute attack has once subsided, but simply with the deformity and stiffness; that is, the result of the disease. A history of the case, that is, sudden onset with high temperature and symptoms of profound intoxication, which may or may

not have been recurrent, are diagnostic of the polyarticular infections and readily distinguishes them from metabolic osteo-arthritis. If for some reason the history is not obtainable, the fact that the joint lesions are not progressive and that the joints are always ankylosed (bony) when the bones are involved, and show no bone changes at all when the bones are free, readily clears up the diagnosis.

When cases cannot be observed for any length of time, or when for some reason the diagnosis is doubtful, the *x*-rays will always definitely

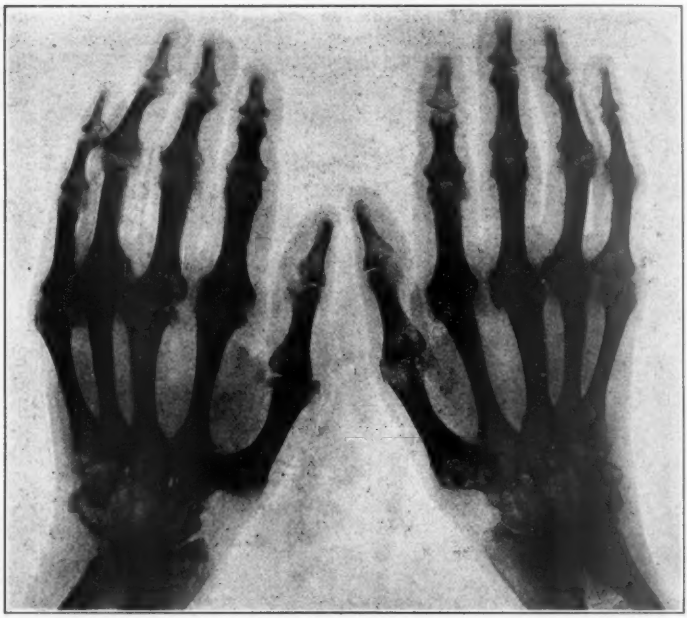

FIG. 9.—Radiogram of the hands in a more advanced stage of metabolic osteo-arthritis than is shown in Fig. 8. The rarefication has spread, some of the epiphyses are distorted, and some of the joints are subluxated. The pressing together of the softened carpal bones gives the appearance of bony ankylosis; but there is no ankylosis, for the joints can be moved passively.

decide it. Good radiograms, particularly of the small joints of the extremity, show very characteristic pictures in the earliest stages of the the disease. Even before there is deformity, a characteristic rarefaction of the bones can be easily made out. At this time, the rarefaction is confined to small circumscribed areas in the epiphysis just below the cartilage (Fig. 8). As the disease advances these areas are found to become gradually larger (Figs. 9 and 10) (more and more bone becoming absorbed), and in the case of the smaller joints the epiphysis, as a whole, may finally disappear. This peculiar form

of rarefication differs radically from that shown by x-ray pictures in the polyarticular forms of infectious osteo-arthritis. In the latter it is diffuse from the beginning, not infrequently involving the shaft (Fig. 11). When recovery is not complete in the later stages it is always accompanied by periosteal outgrowth and bony ankylosis (Fig. 12). In the early stages of the other forms of trophic osteo-arthritis (senile and neurotic osteo-arthritis) the same form of rarefication occurs; but as these forms of joint disease practically always involve the larger joints, the changes are not so readily made out. The senile and neurotic forms of osteo-arthritis are easily differentiated from metabolic osteo-arthritis by the presence of periosteal

FIG. 10.—Radiogram of the hands shown in Fig. 1, an advanced case of metabolic osteo-arthritis in a child, with extreme rarefication. All the joints can be passively moved. Here as in all cases of metabolic osteo-arthritis there is no proliferation or hypertrophy.

outgrowths of various kinds, the so-called hypertrophic processes. As a result of the softening of the bones in metabolic osteo-arthritis, the articular ends of the bonds, particularly of the large joints of the lower extremity, become distorted in the later stages of the disease. This is, of course, readily made out in the x-rays. At times the softened bones spread as the result of weight bearing, and occasionally, particularly in the knee, the thin edges of the articular surface turn over. These lips have been mistaken for periosteal or cartilaginous outgrowths, in the interpretation of the x-ray picutres, by some observers. Careful observation in conjunction with the examination of pictures of other joints will prevent such an error.

If we combine the characteristic clinical phenomena with the *x*-ray findings in metabolic osteo-arthritis, we have a symptom complex which is pathognomonic. Hence, if a given case of joint disease is polyarticular, involving the peripheral joint first, with a marked tendency to be symmetrical, if the course of the disease is gradually progressive, new joints being involved from time to time; if the physical joint changes begin with swelling which is followed by gradually increasing deformity; and if the radiograms show the

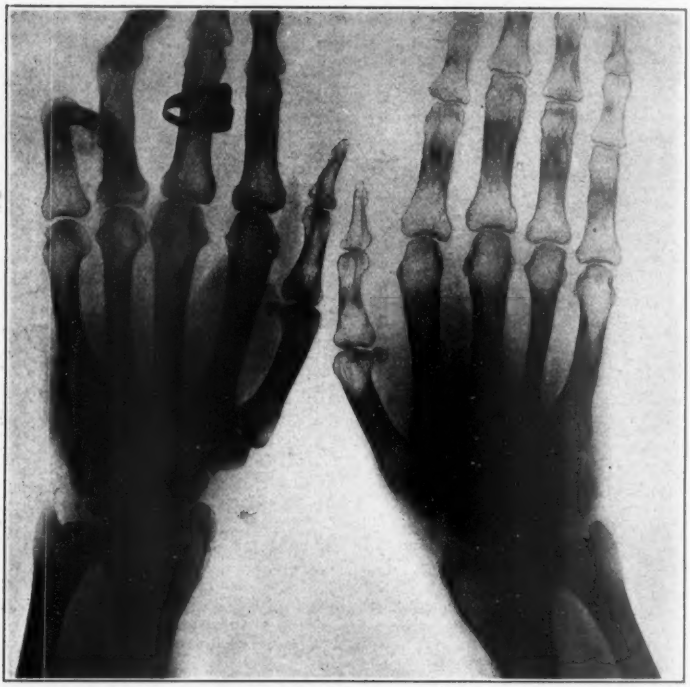

FIG. 11.—Radiogram of the hands in infectious osteo-arthritis, showing the tendency of the rarefication to involve the shaft immediately. The left hand was first affected, and the disease, which had here run its course, has lead to bony ankylosis in the fourth and fifth fingers.

peculiar punched-out rarefication in the early stages, and the absorption and distortion in the late stages, without the presence of proliferative processes or bony ankylosis, no matter what other condition may be present, it is absolutely certain that the joint disease is metabolic osteo-arthritis. And only when this combination of symptoms is present are we dealing with this condition.

As time goes on, and we become more familiar with the scientific differentiation of joint disease, there is no reason why, with such

striking clinical phenomena, the diagnosis should not be made without the aid of the *x*-rays.

PATHOLOGY. As was said in the beginning, the main cause for the misconceptions which prevail regarding the chronic joint diseases is, that the pathology has not been studied in conjunction with clinical observation. With one exception (Kachel[1]) pathological findings have been described as derived from cases of arthritis deformans or rheumatoid arthritis, without an adequate, or, in some instances, without even a hint of the clinical history of the case. Hence, as the ideas of what was arthritis deformans or rheumatoid arthritis differed, and as the pathological specimens were often obtained from totally different conditions, it was only to be expected that misconception should ensue.

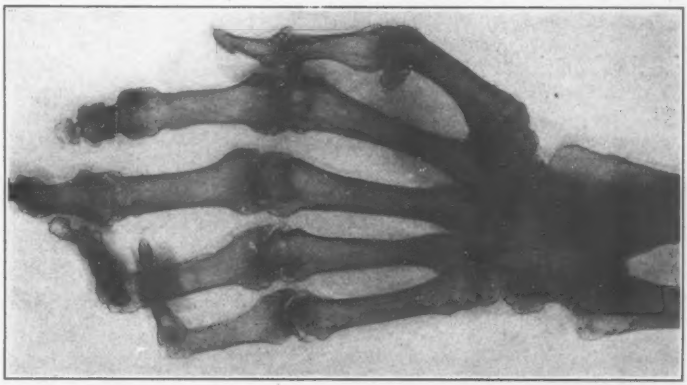

FIG. 12.—Radiogram of the hands of a case of polyarticular infectious osteo-arthritis, which ran its course many years ago. Bony ankylosis and diffuse rarefication of the shaft have occurred.

In the present instance particular care was taken to study the pathology only in such cases in which the clinical diagnosis was unmistakable and corresponded to the symptom complex here designated as characteristic. The pathological study here presented is based upon six cases which came to autopsy. About thirty joints were carefully examined, both macroscopically and microscopically. Besides the cases in which there was a complete autopsy, I have examined individual joints, ten in number, from various sources in which the clinical diagnosis was positive.

In the majority of instances the description of the pathology of metabolic osteo-arthritis begins with a description of the changes in the synovial membrane or the cartilage, and I believe nearly all authorities are of the opinion that the disease begins in one or the

[1] Untersuchungen über Polyarthritis Adhesiva, Ziegler's Beiträge, Band xxxiii.

other of these structures. Under these circumstances, one who studies the pathology of metabolic osteo-arthritis is surprised to find the cartilage quite normal and the capsule with insignificant changes during the early stages of the disease. Upon opening a joint which had shown distinct abnormality during life (swelling, pain, deformity), one often finds little besides capsular irritation and a small amount of effusion in the interior. At this stage, though the cartilage is apparently quite normal, the articular ends of the bones, particularly those of the larger joints of the lower extremity, often show considerable distortion. Moreover, if the epiphyses are cut into or sawn, it is found that they are decidedly softer than normal; and if the disease is at all advanced, they may be cut readily with a scalpel.

If a section of the articular end of the bone is examined, one finds the marrow more red, and the trabeculæ of the spongiosa diminished in number and thinner than normal. During the early stages the bone atrophy is distinctly subchondral, but it gradually advances and finally involves the whole epiphysis. In a majority of cases at an early stage, one can discover with the naked eye, or at any rate with a low-power magnifying glass, minute cavities situated in the subchondral region of the epiphysis within, or at the edges of the bone trabeculæ. These are bone cysts and they vary in size, being of course larger and more numerous as the diseases advances. The more recent ones are apparently filled with a mucilaginous material; the older ones are empty. Besides the cysts there are in the subchondral and later in the deeper portions of the epiphysis as well, opaque areas resembling foci. These focal areas are composed of more or less dense connective tissue. In the later stages these areas of connective tissue have increased considerably, and frequently have coalesced to form extensive areas. In the terminal stage the connective tissue not only invades the deeper portions of the epiphysis, but when the cartilage has in part, or, as a whole, disappeared (which is usually the case), it also invades the interior of the joint.

As has been said the cartilage shows no changes during the early stages of the disease. Indeed, in joints which, because of muscular contraction have been held stiff for a long time, it may be covered to some extent by connective tissue, without showing marked signs of degeneration or ulceration. In such cases the connective tissue is not derived from the cartilage by splitting and fibrillation as the previous writers upon this subject suppose, but can be traced to the zone of capsular insertion from which it originates. It exactly resembles the connective tissue (loosely vascular), which appears in all joints that have been immobilized (without bony ankylosis) for a long time. And I have convinced myself that in cases of metabolic osteo-arthritis, in which it is present before the cartilage has been affected, it is due to the immobilization and is not a part of the pathological process. That it is not part of a proliferative process which beigns in the capsule is evident from the fact that it is frequently present when the

capsule shows no signs of proliferation anywhere else. (It is then exactly analogous to the connective tissue which is found between the joint surfaces in the normal joints of animals which have been immobilized for experimental purposes. In such cases the joint motion is found limited when the retention dressing is removed; this limitation of motion is found to be due to muscular contraction just as in metabolic osteo-arthritis; similarly when the tendons are cut free motion is again possible. In the interior of the joints the cartilage is found covered with a layer of loose, somewhat vascular, connective tissue which exactly resembles that described above).

As the disease advances the subchondral changes increase, and the nutrition of the cartilage being impaired it becomes involved in the pathological process. It loses its lustre, splits, ulcerates, and finally disappears altogether. In the joint disease under discussion, whatever may be the case elsewhere, the joint cartilage never shows any signs of proliferation. It is true that at an early stage, on microscopic examination, one occasionally finds cell multiplication to a limited extent, but here, at any rate, the cellular increase is simply a prelude to degeneration, and there is never an increase in the amount of the cartilage to be made out macroscopically. The chondromas which are described as occurring in arthritis deformans (which by the way are not chondromas at all, but consist of uncalcified osteoid tissue derived from the periosteum) do not occur in metabolic osteo-arthritis. Nor are periosteal outgrowths of any kind ever to be found.

The degeneration of the cartilage varies according to the location and extent of the disease in the underlying bone. At times it appears focal, but close examination will always reveal changes extending some distance from the supposed focus. Naturally, degenerated or degenerating cartilage loses its functional power and hence suffers from pressure. For this reason the so-called cartilaginous ulcer appears where the articulating surfaces are held firmly together by muscular contraction. As soon as a defect occurs it becomes filled with connective tissue. This connective tissue, which comes from the degenerating spongiosa, soon fills up the gap in the cartilage and invades the interior of the joint, where it comes in contact and coalesces with the connective tissue derived from the border of the capsule. In this wise the joint cavity becomes more or less completely filled with connective tissue; and if the cartilage degenerates completely (the usual condition in the terminal stages of the disease), the articular surfaces of the opposing bones are separated, or, more correctly, united by connective tissue. This new-formed connective tissue is not dense, but loose and vascular. There are few round cells within it, and none in the neighborhood. It does not involve the capsule, which indeed may be rudimentary. It shows no marked tendency to contraction, so that it does not cause ankylosis or even marked joint stiffness. When there is limitation of motion in these

cases, it is due to muscular contraction and disappears when the tendons are cut.

The capsular changes, supposed by many to be the earliest, are really insignificant. In the joints in which the disease is just beginning, there is simply a small amount of effusion and some injection. At times there is some hypertrophy of the synovial fringes—but as far as my own cases go, there is never the enormous villous formation described by some authors. Later, the capsule degenerates with the other parts of the joint. It becomes lax, more succulent; the inner surface loses its lustre; the synovial fringes which may have been somewhat hypertrophied during the earlier stages undergo fatty degeneration; and, finally, only a few shreds of degenerated capsule mark its former location.

Thus, macroscopically, the disease manifests itself by a degeneration and gradual disappearance of the joint structures. The bone ends, which in the early stages are distorted and deformed, in the

FIG. 13.—Femur from a case of metabolic osteo-arthritis. The head of the femur is almost entirely absorbed; both epiphyses are extremely delicate and break between the fingers like eggshell.

later stages become rudimentary, and in the small joints disappear entirely. The rarefication and bone absorption are best demonstrated in the dried specimen. Thus, Fig. 13 represents the femur of an advanced stage of metabolic osteo-arthritis. The femoral head is rudimentary, and the bony tissue is so thin and delicate that it breaks like eggshell between the fingers. Fig. 14 shows a cross-section of the head of the femur in another less advanced case, showing distortion, rarefication, and cyst formation. Unlike the cases of monarticular trophic osteo-arthritis, in which the articular ends of the bones are also somewhat rarefied and softened, there are never signs of proliferation (pseudohypertrophic processes) in metabolic osteo-arthritis.

In the terminal stages of the severe cases the small joints almost completely disappear. The opposing articular surfaces are separated by connective tissue, there is no joint cartilage, no joint cavity, and the capsule, ligaments, and even the tendons in the neighborhood are reduced to mere shreds.

Microscopic Examination. Osteomalic and osteoporotic changes are present side by side, and they differ in nowise from those found in other forms of bone degeneration. There can be no question regarding the softening, for on staining with hematoxylin and carmine certain areas of what should be calcified bone, and, therefore, take the carmine stain, are colored blue (hematoxylin) instead. In such areas the bone-cell cavities are larger than normal. The cells show various degenerative changes. At times they are larger than normal, but take the stain with difficulty; later they are shrivelled, the processes are absent, and finally they completely disappear.

The ground substance becomes cloudy and granular. The bone-cell cavities increase in size, a number of them coalescing to form larger cavities filled with a mucilaginous fluid, thus forming the cysts. As the process advances, the bone cysts increase in size, more and more of the softened bone substance being absorbed; thus the

FIG. 14.—Section of the head of the femur, showing the distorsion and the rarefication.

trabeculæ become much reduced in thickness, and finally many of them completely disappear. Lacunar absorption also occurs, and Howslip's lacunæ are to be seen upon the surfaces of the trabeculæ.

The marrow shows marked signs of degeneration. The fat is diminished, and in the earlier stages is displaced by a mucin-like fluid. Later the connective tissue fills the spaces between the degenerating trabeculæ. In a like manner connective tissue fills the cysts forming the opaque areas seen with the naked eye, and finally, after the disappearance of the cartilage, it penetrates the interior of the joint.

The changes in the cartilage are those which occur in all forms of degeneration in this structure. Proliferating cells occur in the early stage, but these are comparatively few in number and no doubt

simply usher in the degenerative process. The cells assume various abnormal shapes, are stained with difficulty, and ultimately disappear altogether. The cell cavities enlarge, the ground substance loses its hyaline character, becomes granular or fibrillated, and ultimately splits and loses its connection with the bone. In those situations where there is pressure, at times also in other places, the articular ends of the bones become denuded in somewhat circumscribed areas, the so-called ulceration of the cartilage. Such defects in the cartilage become filled in with the connective tissue from the bone below, and and to a lesser extent with that which comes from the border zone of the capsule. These defects or ulcers are not caused by the active invasion of the connective tissue from the interior of the joint into previously healthy cartilage, as described by many writers. This is improbable in any case, because normal cartilage cannot for physiological reasons be invaded by connective tissue. In the present instance there is evidence besides, in direct contradiction to such a method of invasion. In the first place, the bone changes are found to be present both macroscopically and microscopically before the cartilage or capsular changes. In the earlier stages of the disease the capsule and cartilage are not involved, whilst the bone degeneration can be readily demonstrated, if not with the naked eye, certainly with the microscope. If the process is carefully followed it is found that the cartilage begins to degenerate at a stage when the amount of connective tissue, particularly that in the interior of the joint, is insignificant. And, finally, if a number of joints are examined, one is sure to find defects in the cartilage which have not as yet become filled with connective tissue. In the majority of instances, the connective tissue in the ulcers can be directly traced to the bone, and as the joint interior only becomes quite filled with connective tissue in the terminal stages of the disease, considering the nature of the process generally, it seems to me only plausible to assume that it originates within the epiphysis.

The capsule shows no characteristic changes. I have never been able to find the enormous proliferation of the villi spoken of by some authors. I am fully in accord with Shuchardt in this respect. Aside from a slight sign of irritation in the early stages, there is a gradual atrophy of the capsule and ligaments, with or without some indication of fatty degeneration.

Thus the joints in metabolic osteo-arthritis present pathological changes which correspond and readily explain the clinical phenomena. The earliest changes are bone changes, and these early bone changes can readily be demonstrated by x-rays during life. The rarefication which is shown by the radiograph to be subchondral and somewhat circumscribed (punched-out rarefication) in the early stages, corresponds to the osteomalic and cyst-like osteoporotic condition to be seen in the postmortem specimens. Proliferation processes are never seen during life, and they are never found when the joints are examined after death.

The clinical phenomena indicate that the condition is one of gradual joint degeneration, and the postmortem findings readily bear this out. As a matter of fact, the condition presents a pure form of atrophic degeneration, as was indicated by Shuchardt when he classed this condition as an atrophic joint inflammation. That it is not an inflammation, however, is evident from both the symptoms during life and the pathological changes in the joints.

In metabolic osteo-arthritis we have, then, a perfectly distinct joint condition which can be distinguished from all other joint conditions both clinically and pathologically. Having decided this point, we are in position to inquire whether this joint condition is of itself a disease, secondary to some other disease, or a part of a distinct general condition. Having constantly in mind that whatever the concomitant phenomena, to be spoken of presently, the joint condition in every case remains exactly the same and corresponds in its diagnostic and pathological features to those here detailed as characteristic of metabolic osteo-arthritis, we proceed to the discussion of—

The General or Constitutional Symptoms Present in Patients with such a Joint Condition. A fairly large percentage of cases shows no definite general abnormality of any kind, except a variable degree of cachexia and secondary anemia throughout the course of the disease. In the milder cases the anemia and emaciation are not very marked, and increase very slowly. In such cases the internal organs show no clinical signs of abnormality whatever. The joint condition progresses slowly and gradually for a number of years, may remit occasionally or become quiescent, and after a variable amount of crippling the patient finally succumbs to some intercurrent malady. In the severest forms, the joint condition progresses rapidly and the cachexia, emaciation, etc., become extreme; and when the external conditions are unfavorable the individual, after a few years of suffering, becomes marantic and dies. Between the mild and the extreme cases there are all grades. In another class of cases, there is a slight rise in temperature in the beginning which remains, with slight remission, continuous for a long time. In these cases the joint condition differs in nowise from that in the cases without fever, and the joint disease continues to progress in the afebrile stage. This, aside from the fact that the joint disease begins insidiously, readily differentiates these cases from the polyarticular infection in which the progress of the joint condition always subsides with the subsidence of the temperature and constitutional disturbance.

Increased pluse rate, even tachycardia, is not an uncommon symptom in both the febrile and the afebrile cases. It is sometimes severe enough to be apparent to the patient, who then complains of palpitation. Such individuals are apt to be, but not necessarily, troubled with symptoms of functional nerve derangement. In some

there is only slight nervousness, but in others there is marked irritableness, abnormal anxiousness, and insomnia. But nervous irritability and functional nervous troubles generally are not particularly characteristic of those with increased pulse rate; such symptoms are common in metabolic osteo-arthritis without tachycardia. That intelligent people who are helplessly crippled should become hypochondrical is not surprising, and does not imply, as some observers would have it, a definite derangement of the higher nerve centres.

Muscular atrophy of a more or less general nature is a marked and constant symptom in osteo-arthritis. To a large extent it can be ascribed to the general emaciation and the causes, whatever they may be, which usually cause this condition in other joint diseases. But in many cases it is so extreme and manifests itself by weakness so early (even before there are perceptible changes in the joints), that it seems not unlikely that other factors besides are influential in its production. In nearly all cases the reflexes are exaggerated. This is to be expected along with other functional nervous derangements. Of a much more specific character is fibrillar contraction which occurs in many cases. This symptom is present when the disease is well advanced, and manifests itself when the muscles are at rest and in action.

According to numerous French observers skin lesions are common in patients suffering from metabolic osteo-arthritis. But from my own observations, which are in accord with those of Pribrim, I have not, with one exception, found them more frequent than one could expect in otherwise normal individuals. Trophic conditions of the nails are occasionally present, but they are not distinct or frequent enough to be considered characteristic. Glossy skin, spoken of by some authors as a characteristic symptom, must be rare, for I have not seen it once in an undoubted case of metabolic osteo-arthritis. On the other hand, I have seen it several times in severe polyarticular infectious osteo-arthritis, and for this reason I think many if not all the cases reported must be based upon a faulty diagnosis. The same seems to be true of the so-called rheumatic nodes. In none of the cases of joint disease I have seen, in which nodes were present, was the joint condition metabolic osteo-arthritis.

Œdema and even scleroderma have been reported. The scleroderma I have not seen; it must be a rare condition, but in a number of cases œdema was present. In these instances I have had the impression that the œdema which occurs in patients without cardiac or kidney lesions, was similar if not analogous to that which occurs in certain neuroses.

A very peculiar and interesting condition of the fingers occasionally presents itself in these patients. The abnormality appears to be due to some change in the skin, and for this reason is discussed under this heading; but in reality it is due to atrophy of the bones and subcutaneous tissues, the skin remaining intact. In consequence

the skin hangs loosely over the fingers, and in severe cases the effect of a worn glove is strikingly reproduced. Some authors have considered this condition to be due to an œdema which, after stretching the skin, has disappeared; but as I have known it to occur in cases in which no œdema had been present, for this as well as other obvious reasons, this explanation is more than improbable. Moreover, in just such cases the extreme atrophy of the bone can be demonstrated by the *x*-ray pictures.

Since the theory of uric-acid intoxication has been abandoned, there remains little to be said regarding the condition of the urine in cases of metabolic osteo-arthritis. So far nothing characteristically abnormal has been found. In the terminal stage of the disease, in children, albumin is present in some cases. It is absent in the majority of the cases, however, and its relation to the condition, if there is one, has not been ascertained.

In children, metabolic osteo-arthritis occurs in connection with two apparently distinct constitutional conditions. One exactly corresponds with that of the afebrile type in adults. The other is a very characteristic condition which, with some evidently different conditions, is known as Still's disease. In 1897 Still described what he considered a characteristic joint disease of early childhood, which manifested itself by the gradual onset of more of less symmetrical joint swelling, enlargement of the glands and the spleen, and fever. According to Still, the disease is progressive and gradually involves all the joints of the body. Since then, all cases of polyarticular joint swelling with fever and glandular enlargement have been designated Still's disease. Now, as has been indicated, certain forms of polyarticular infection in children are characterized by polyarticular nodular swelling, which may or may not be symmetrical. In these cases there is often glandular swelling, and sometimes the spleen is also enlarged and palpable. These cases are usually called Still's disease. Whether it is proper to call them so remains for Still to say, for he considers the condition that bears his name infectious.

It is certain, however, that these cases differ radically from a definite condition occurring in children, in which the joint disease, whatever the general condition, is certainly not infectious. I have seen ten such cases with two autopsies. The joint changes are purely degenerative and correspond exactly with those of adult forms of metabolic osteo-arthritis. Of course, owing to the preponderance of the cartilage in young children, the bone changes are not so definite and cannot be made out in radiograms.

The disease comes on insidiously, symmetrically involves the peripheral joints first, thence gradually procedes to those of the trunk, and finally all the joints of the body become affected. In these cases there is very little or no pain, and the children rarely complain of it, unless compelled to walk or are roughly handled. There is moderate but general glandular enlargements. Not only the glands in the

neighborhood of the affected joints are involved, but all the glands take part in the process; and at autopsy I have found decided swelling of the bronchial and mesenteric glands. The spleen is invariably enlarged and palpable. At times the liver is also enlarged, and in some cases extends far down below the free border of the ribs. (Fig. 15 shows a child in whom the liver and spleen are so large that although there is no ascites, the abdomen is markedly protuberant.) There is a moderate continuous temperature, with secondary anemia and cachexia.

FIG. 15.—Case of metabolic osteo-arthritis in a boy. (The hand is shown in Fig. 4.) The liver and spleen are so large that they cause marked protuberance of the abdomen.

Whether Still includes cases of this nature with the polyarticular infections, I cannot quite make out. In the conditions I have outlined above, the fingers were always involved; this does not seem to be so in the cases reported by Still and others.

From the study of the general symptoms, it is evident, that while the joint condition remains uniform, the constitutional symptoms vary within wide limits. It is quite improbable that a primary uniform joint disease should be responsible for such variable general

symptoms, much less such totally distinct constitutional conditions as, for instance, the two forms which occur in children. We may, then, without resorting to further argument, conclude that the joint disease is not a primary local condition causing secondary general symptoms. The next question to decide is, Is the joint condition secondary to some specific general abnormality. That there is some morbid condition which affects the metabolic processes is evident; the cachexia, the effect upon the nervous system, upon the heart (tachycardia), and even upon the vascular system (for vasomotor disturbances have been observed in a number of cases), the symmetrical and progressive character of the joint lesions all speak for this. However, although it cannot be denied that some metabolic disturbance is responsible for the joint and some of the other symptoms, this does not necessarily prove we are dealing with a uniform and specific general disease as a cause.

On the contrary, the variability of the general symptoms plainly indicate that this cannot be the case. Indeed the fact that perfectly typical cases of metabolic osteo-arthritis are known to occur in the course of widely differing diseases, plainly indicates that the constitutional condition, whatever its relation to the joint condition, may owe its presence to totally distinct and opposite morbid influences.

Whatever may be the case with the other skin diseases, it is certain that individuals who suffer from psoriasis show a marked tendency to have trophic joint disease. And although the lesions in such cases are not always typical metabolic osteo-arthritis, so many of them are that we must conclude, as was suggested in one of my previous papers, that the two conditions are in some way related. Their relation to each other or to the common cause need not again be discussed. That the pathogenesis and cause in cases of metabolic osteo-arthritis with psoriasis is different from that of metabolic osteo-arthritis without this skin lesion seems a reasonable conclusion. For it is quite unlikely that a given pathogenic factor should directly produce such a typical skin lesion in one case, and be present in another without causing such lesions.

Basedow's disease is another distinct disease in the course of which metabolic osteo-arthritis may develop. In this instance the relation to metabolic osteo-arthritis has been erroneously interpreted in a number of cases reported. So-called rheumatoid arthritis and Basedow's disease have been thought to co-exist, when, as a matter of fact, the Basedow followed a general infection with joint symptoms (infectious polyarthritis or osteo-arthritis). What I refer to here, however, are typical cases of metabolic osteo-arthritis, which come on in more or less typical examples of exophthalmic goitre. I have seen two such cases. In a third case, besides the typical joint disease, there were exophthalmos, large liver, spleen, and glands, with tachycardia. A similar case has been reported by Dr. Manges.[2]

[2] Mt. Sinai Hospital Reports, vol. i.

That tachycardia and nervous symptoms occur in connection with metabolic osteo-arthritis was, I believe, first pointed out by Spener; and the similarity of these symptoms with those of Basedow's disease has since been suggested by a number of authors. Besides a number of cases with typical Basedow and typical metabolic osteo-arthritis have been reported. Here, again, the constitutional symptoms vary greatly. From the cases previously referred to, in which there is simply increased pulse rate, to the cases with distinct tachycardia, exophthalmos, large thyroid (typical Basedow's), there are various grades of constitutional disturbance suggesting this condition.

Still more striking, however, is the fact that typical metabolic osteo-arthritis may occur in the course, and apparently as the result of pulmonary tuberculosis: not that the conditions generally spoken of as tuberculous rheumatism are always cases of this joint disease, for all forms of joint disease due to direct infection, acute toxemia, and trophic conditions have been so designated. As far as trophic or degenerative conditions of the bones and joints are concerned, three distinct forms occur with pulmonary tuberculosis; these are: (1) Monarticular forms of trophic osteo-arthritis (senile type). (2) Hyperplastic peri-ostitis or ostitis (osteo-arthropathie hypertrophiante pneumique, Marie) (so-called club fingers). (3) Metabolic osteo-arthritis. That so many diverse conditions should occur under these circumstances, is not surprising when it is considered that the tubercle bacilli secrete no toxin, but cause toxemia or general disturbance because of the disintegration of the tubercle bacilli themselves. As the tubercle bacilli are complex bodies, it is to be expected that their disintegration and absorption should cause variable symptoms and conditions.

It is plain, then, that metabolic osteo-arthritis occurs not only in individuals who present variable constitutional symptoms, and, therefore, no doubt have variable constitutional abnormalities, but it also occurs in the course, or as the result of totally distinct and well-recognized diseases. Hence it cannot be due to a distinct and uniform general disease.

Nor to judge from the totally distinct character of the morbid conditions with which it is associated, can it be due directly to the various causes which induce these conditions. For it is quite unreasonable to suppose that a morbid condition like that due to the tubercle bacillus, which either causes changes due to direct invasion or to a toxemia, which necessarily involves some irritation (degeneration with proliferation, or even inflammation), should in certain isolated examples induce such a purely atrophic degeneration as occurs in metabolic osteo-arthritis; still less so, that such a pathogenic factor should directly induce the same pathological changes, as do others so totally different, as those which are responsible for the other conditions with which metabolic osteo-arthritis is known to be associated.

The only reasonable supposition is that all these conditions are active in producing an analogous general disturbance of the organism which in turn causes the joint degeneration. Indeed, it has been suggested that a general nervous derangement is the cause of it. But this cannot be true, because derangements of the nervous system, diseases of the spinal cord or the brain, or peripheral nerve lesions do not cause conditions like metabolic osteo-arthritis, but others, such as trophic osteo-arthritis of the senile type.

On the other hand, differing as they do in their origin and nature, the conditions, known or unknown, with which metabolic osteo-arthritis is associated, all have one thing in common. This is their deleterious influence upon the general nutrition. It matters little in what way this influence is exerted, as far as the tissues are concerned; upon them the result is the same, viz., inadequacy of the nutrition. In metabolic osteo-arthritis, the joint condition, a pure atrophic degeneration, exactly corresponds to what one would expect under such circumstances.

As a matter of fact, if we can rely at all upon the principle of general pathology, the changes which are typical of this condition could only be caused by a purely nutritive anomaly. Hence the conclusion that metabolic osteo-arthritis is due to a metabolic derangement which seriously impairs the joint nutrition is inevitable.

Whether or not the vice of the metabolism is of a peculiar kind, it is impossible, in the present state of our knowledge, to say. It is certain, however, that no toxic substance in the circulation can directly cause the joint changes. If a toxemia or auto-intoxication is present, its toxic effect is not exerted upon the joints directly, but indirectly through the impaired nutrition. All the toxemias, acute and chronic, with which we are familiar, when they act directly, induce similar changes in the bones or joints. When they act acutely they cause acute inflammation; when chronic they cause hyperplastic periostitis or ostitis or degeneration with proliferation in the joints (toxic polyarthritis or osteo-arthritis of the senile type).

But if the joint condition is purely one of the nutrition, it might be asked, Why should the joints and bones alone be involved? This question is readily answered. In the first place, the bones and joints are not the only tissues involved. In the severe forms the tissues in the neighborhood of the joints are appreciably atrophied. There is general emaciation and secondary anemia. The general musculature is markedly atrophied. That the internal organs show no changes is by no means certain; they have never been carefully examined. Finally, the fact that the bones are so strikingly involved, is not at all surprising when it is remembered that the bones are unusually sensitive to changes in the general nutrition as, for example, the marked bone changes in rachitis, the atrophy of senility, and even physiological conditions, the bone softening in puberty, juvenile osteo-arthritis, lateral curvature, etc., and the osteomalic changes in pregnant women.

From the study of metabolic osteo-arthritis here undertaken we are justified in drawing the following conclusions: (1) Metabolic osteo-arthritis is a distinct pathological condition of the joints, which can easily be recognized clinically; (2) it is not, however, a primary joint disease causing secondary general symptoms; (3) nor is a uniform specific general disease responsible for it; (4) it occurs in connection with a number of distinct clinical conditions, some of which are known to be specific diseases; (5) the joint disease is not due directly to the conditions with which it is associated, but is due to their deleterious influence upon the general nutrition.

How the metabolism is affected or what changes it undergoes has not been determined. What is certain, however, is that the changes in the joint are passive: simply an atrophy which can only be induced by inadequacy of the nutrition.

For these reasons the joint disease here discussed has been grouped with the nutritive or trophic joint diseases. In order to distinguish it from those conditions which cause local changes only it has been termed metabolic, and to distinguish it from the rather uncommon metabolic conditions which cause synovial changes only, it has been called osteo-arthritis.

Thus, metabolic osteo-arthritis is a chronic osteo-arthritis due to a vice of the metabolism caused by a number of conditions, organic or functional; insidious in onset; symmetrically involving new joints toward the trunk, it gradually leads to more or less deformation and crippling. The *x*-rays shows circumscribed bone rarefication in the early stages, and a more or less complete absorption of the epiphyses in the later stages, but never proliferation or bony ankylosis. Pathologically, beginning in the bone, there is a pure atrophic degeneration of all the joint structures.

TREATMENT. Up to the present time the prognosis in metabolic osteo-arthritis was considered hopeless as regards the recovery from the joint condition. To be sure, it was known that in certain cases the disease became quiescent; but no consistent effort to improve the condition, as far as I know, has been successful. These individuals are among those who have spent their time visiting one resort after another without deriving benefit from any. Cures have been reported, but those who recovered were evidently not suffering from metabolic osteo-arthritis.

In reporting results of treatment in these cases, the sine qua non is the diagnosis. To say one has cured a case of rheumatoid arthritis is to say nothing at all—for the case may have been one of infectious polyarthritis which could have recovered without specific treatment of any kind. So in the cases, to speak only of recent examples, reported by Hoke and Andrews, which are said to have been cured by the use of kifolac. These cases comprised all forms of joint disease, monarticular, polyarticular, trophic, and infectious, so that these statistics are practically useless. Whether or not kifolac is

useful in metabolic osteo-arthritis, I have not been able to determine. In the few cases I have seen which were treated with it, I could see no improvement; but these cases were not in my own care, and apparently were not systematically treated. On the other hand, I have had uniformly good results with the use of thymus gland extract.

Some years ago I began to use it, because of the influence of the thymus upon the development of the bones, as was shown by Basch[3] in his experiments upon animals. I first used it in children in whom I found it had a very remarkable effect. In children with the metabolic osteo-arthritis with large glands and spleen, the joint disease soon became quiescent, and children who had not been upon their feet for from six months to over a year were again able to walk. That the restoration was due to the thymus and not to natural causes, was proved by the fact that the joint symptoms soon returned when the gland treatment was omitted. Good results were also obtained in children without glandular swelling, and in adults. In adults the effect upon the general nutrition is very marked. Patients who are extremely emaciated soon begin to take on flesh, and the muscular power is greatly increased. In the earlier stages of the disease the improvement is more rapid and definite. In the later stages large doses must be continued for some time before there is apparent benefit.

Of course it is quite hopeless to attempt restoration of joints which have been more or less completely absorbed. But in these cases the improvement in the general condition and increased weight is of decided benefit to the afflicted individual. In long-standing cases muscular contraction continues even after all joint symptoms have subsided. Such muscles have been permanently shortened, and the deformity so caused must be corrected by tenotomy. To attempt to stretch these tendons is dangerous, because such efforts are more likely to result in the fracture of the softened bones than in the stretching of the tendons. I have seen this accident a number of times.

My method of proceeding in these cases is as follows: The thymus is given immediately. I usually begin with two 5-grain tablets, thrice daily. In two weeks the dose is increased to three tablets, and after a few months three tablets four times a day are given. The patient is kept at rest until all symptoms of active joint disease have subsided. I then begin passive motion in all the affected joints. This is carefully done at first and gradually increased until I have an arc of free motion which is only limited by the shortened tendons. Massage, which is often painful, is unnecessary and may even be harmful. My next step is to get the patient on his feet. This is sometimes a tedious affair; for patients, particularly adults, are

[3] Jahrbuch f. Kinderheilkunde, Band xiv.

timid at trusting themselves at first. But by persistence the patient eventually gains confidence, and finally is able to get around as well as deformity in the lower extremity will permit. I have found it much more satisfactory, when I have the proper assistance and the patient the means, to take them into a private institution whilst they are learning to walk. Public hospitals are not suitable, because in them there are neither the trained assistants nor the time for this kind of work. A persevering intelligent mother can usually do more with a child than anyone else.

As soon as the patient is able to be upon his feet or use his joints without the appearance of joint irritation, all contracted tissues are divided with the tendome and the deformity is corrected. This, of course, requires immobilization for three or four weeks; but with light plaster-of-Paris bandages it does not preclude the use of the lower extremities. A few days after the operation the patient is again induced to be about, and he is usually able to hobble around quite comfortably with crutches or a cane until the bandages are removed.

With such treatment all but the most severe cases, which have existed for a long time, can be definitely improved. Often the patients recover sufficiently to be about and attend their avocations. The treatment, however, requires patience, a definite knowledge of the condition, and time; without these only in the very mild cases can one be successful.

It must not be supposed that I consider the thymus extract a specific for the cure of this condition. The nature of the disease, as it has been enunciated in this communication, precludes such an idea. Moreover, the fact that in children the enlargement of the glands, liver, and spleen is not at all affected, although the joint condition is markedly improved, shows conclusively that its action is not specific, as far as the original constitutional condition is concerned. The thymus acts simply as a stimulant to the nutritive processes, and probably in a measure counteracts the deleterious influence of the causative condition.

In conclusion, I take pleasure in thanking the following gentlemen for the use of clinical material: Dr. W. R. Townsend, Dr. V. P. Gibney, of the Hospital for Ruptured and Crippled; Dr. E. Libman and Dr. M. Manges, of the Mt. Sinai Hospital; and Dr. Albee and Dr. Cole, for *x*-ray work done for me. The majority of my cases were seen outside of hospital practice, and I am indebted to many of my medical friends for referring them to me.

PRIMARY SPLENOMEGALY OF THE GAUCHER TYPE.

A REPORT ON THE SECOND OF FOUR CASES OCCURRING IN A SINGLE GENERATION OF ONE FAMILY.

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When our report of the pathological conditions found in one of the fatal cases of the family suffering from primary splenomegaly of the Gaucher type was published in March, 1905,[1] we were working at the organs of the sister of the patient who formed the subject of our report, and had promised to publish the pathological findings in this second case. After many delays we have finally succeeded in bringing our findings to publication.

The clinical histories of these two cases have been recorded.[2] The history of the second case may here be succinctly continued to the time of her death in September, 1904: Increasing anemia, increasing emaciation, increasing enlargement of the abdomen due to enormously increasing size of the spleen and liver were noted. Outside of a fracture of the third and fourth ribs on the right side, due to a fall in 1902, the patient was never confined to her house. These fractures healed without delay, with a large amount of callus. There were infrequent attacks of epistaxis, more frequent attacks of bleeding from the gums. Occasionally melena was noted, and on numerous occasions the feces gave positive reactions to the guaiac test. Ecchymoses occurred in the skin after the slightest injury. Pains referable to the ends of the femur and tibia were often complained of, but nowhere could bone tenderness be elicited. Sweating and hemorrhagic sudamina became more frequent. The brownish, uniform discoloration of the skin of the face and hands deepened. The hemoglobin gradually diminished to 35 per cent. (Dare instrument), although the red blood count at its lowest was 3,500,000. The white blood count still showed a tendency to leukopenia, the count being 3600 to 5200; no qualitative changes. There were no evidences of jaundice. Bile was absent from the blood serum and urine; the latter contained no urobilin.

Notwithstanding the apparently wretched appearance of the

[1] Primary Splenomegaly, Gaucher Type. Report on One of Four Cases Occurring in a Single Generation of One Family. Amer. Jour. Med. Sci., March, 1905.

[2] Amer. Jour. Med. Sci., April, 1901, and March, 1905.

patient, which suggested a very serious illness, she showed an almost ceaseless activity, attending to domestic and social functions. She made no complaint of feeling ill outside of complaining of dyspnœa. On September 12, 1904, on crossing the street she was hit by a bicycle, which suddenly rounded the corner of the street, and knocked down, sustaining a fracture of the skull and laceration of the brain, from which she died that night.

Postmortem examination, September 13, 1904 (seven hours after death). Body length 155 cm. Marked emaciation; rigor mortis marked. Petechiæ in left conjunctiva, with large hemorrhages under the conjunctiva at the outer canthus. Hemorrhages are also present in the skin of the upper lids on both sides. No jaundice. Diaphragm on the right side at the second space; on the left side at the second rib. Cervical lymph nodes perceptible; axillary nodes not palpable; inguinal nodes perceptible. Small amount of clear, reddish fluid in the abdomen. Marked adhesion of the spleen to the abdominal wall and omentum. The spleen almost fills the entire abdominal cavity, extending about two fingers' breadth below the level of the superior spines of the ilium on both sides. The liver is adherent to the anterior abdominal wall. The small intestines lie below, behind, and to the right of the spleen. The stomach lies between the liver and the spleen, on the right side of the abdomen, the pylorus being situated posteriorly.

Over the occiput is a large hematoma, about 1.5 cm. thick and 7 cm. long. The brain is lacerated on the inner aspect of the frontal convolutions of the right side. Beneath the pia mater on the median surface of the right hemisphere is a large amount of blood. An extensive hemorhrage is also present over the entire external surface of the left hemisphere, and an extensive laceration of the left temporal lobe and third left frontal convolution is seen. The middle third of the median aspect of the right hemisphere is also lacerated. The line of fracture extends from the right posterior lacerated foramen across the transverse sinus to a point 2.5 cm. above and 2.5 cm. to the right of the torcular.

The heart weighs 215 grams. Fairly firm bands between visceral and parietal pericardium. Wall of right ventricle 0.5 cm. thick; left ventricle dilated, wall 1.25 cm. thick; right auricle dilated. Mitral valve slightly thickened, ring somewhat calcareous; aortic valve slightly insufficient (water test); some retraction of the flaps and thickening of their lines of attachment. Slight atheroma of aorta and coronaries. No congenital lesions. Heart muscle is brown in color. The lungs are non-adherent; fairly well expanded; anthracosis; moderate congestion. Bronchial nodes slightly enlarged and anthracotic. The spleen measures 45 x 25 x 13 cm.; and weighs 8.1 kilograms. There is recent and old perisplenitis. The pulp swells above the level of the cut surface. The color, as a whole, is salmon pink with grayish markings. There are no evidences

of Malpighian bodies. Scattered throughout the spleen are large and small elevated areas which are firmer than the main bulk of the tissue. Most of these are red in color, with grayish and yellowish markings; a few are reddish at the margins and yellow at the centre. Besides these, a number of large, yellow, cheesy areas are seen, a few of which are very soft and are surrounded by a capsule. Splenic artery negative; splenic vein atheromatous. Near the hilum are a few small masses of accessory splenic tissue, pale yellowish in color. The liver is irregularly quadrate in form, very much enlarged; weight 3.9 kilograms. The width is 35 cm.; length of right lobe, 30 cm.; left lobe, 18 cm.; greatest thickness, 12 cm. Old and recent perihepatitis. The parenchyma swells above the cut section, is light browinsh in color, with irregular grayish markings. The outlines of the lobules are absent. On the under surface are a number of small hemorrhagic markings. The portal vein and the hepatic veins are negative. The gall-bladder is distended with dark, thick bile, containing a large number of very small, irregularly rounded stones, black in color. The wall of the gall-bladder appears to be normal; the ducts are pervious.

The kidneys combined weigh 270 grams. The right kidney measures 12 x 6 x 3.5 cm.; the left 13 x 7 x 3.5 cm. The left kidney is flattened, its capsule is adherent. The veins of the surface are injected, and a few dark depressions and small cysts are present. The cortex is swollen, and has a yellowish red color. On section the markings are poor; the medullary pyramids are intensely congested. The right kidney shows the same changes as the left, excepting that the medulla is less congested.

The right adrenal is large and flattened, and the medulla appears hemorrhagic. The left shows no changes. The stomach is much dilated; contains curdled milk. The ascending and transverse colon are moderately distended; the descending colon and sigmoid flexure are collapsed. The small intestine presents areas in which the vessels are very much distended and the mucosa swollen. The lymphoid follicles are very distinct and white in color, and especially prominent near the valve. The large intestine shows distention of veins and areas of inflammation, and lymphoid areas similar to those in the small intestine. The pancreas weighs 90 grams. The cut section shows congestion of the veins.

The mesenteric nodes are moderately enlarged; on section they are either entirely yellowish in color or dark red with yellowish markings. The retroperitoneal and iliac nodes, as well as the nodes of other parts of the abdomen, show the same changes as the mesenteric nodes. Some are the size of a pea, others as large as an almond. The iliac nodes are the size of an almond, and on section are either diffusely yellow in color or brownish black with yellow markings. The uterus is atrophic and virginal. There is an old hemorrhagic area in the right ovary, and remains of corpus luteum. The bladder shows

injection of the vessels. The marrow of the vertebræ is normal. The cavity of the femur is filled with soft tissue which is dark red in color, with some yellowish areas.

Microscopic Findings. It may be stated at the outset that the lesions found in this case do not differ materially from those described in our first case, excepting that the changes in some of the organs are more advanced, as a result of the longer duration of the disease.

Spleen. The necrosis in this organ is very advanced. A study of the necrotic areas shows that the nuclei of the characteristic endothelial cells disappear somewhat earlier than the protoplasm. Large masses of endothelial cells are found, whose contours may still be

FIG. 1.—Section of the liver, showing endothelial cells in the meshes of the interlobular connective tissue. In the centre of the field are a few normal liver cells. (Photomicrograph × 250.)

recognized but whose nuclei are absent. Surrounding these necrotic areas are cells in which degenerative changes are apparent but in which the nuclei are regularly seen. A few capillaries are present in the necrotic areas, and small collections of pulp cells may be noted here and there. The hemorrhagic areas in this case are very extensive and are found in nearly all of the portions examined. More pigment is seen in this than in our previous case, and many of the cells are literally crowded with pigment granules. The distribution of the pigment is the same as in our earlier case, though here and there a few small particles are seen in the endothelial cells lining the capillaries. With these few exceptions, the sections present the same appearances that were described in full in our first case.

Liver. The endothelial cells are very abundant in this organ and easily seen. As a rule, they are situated in the meshes of the interlobular connective tissue (Fig. 1), but a large number are also present in the lobule proper. In this situation they lie between the liver cells, without exerting any apparent pressure effects upon the latter (Fig. 2). With the low power the picture is that of a cirrhosis. A few of the characteristic endothelial cells are seen in the lumen of one large vein in the interlobular connective tissue. The pigment is the same as that described in our former case.

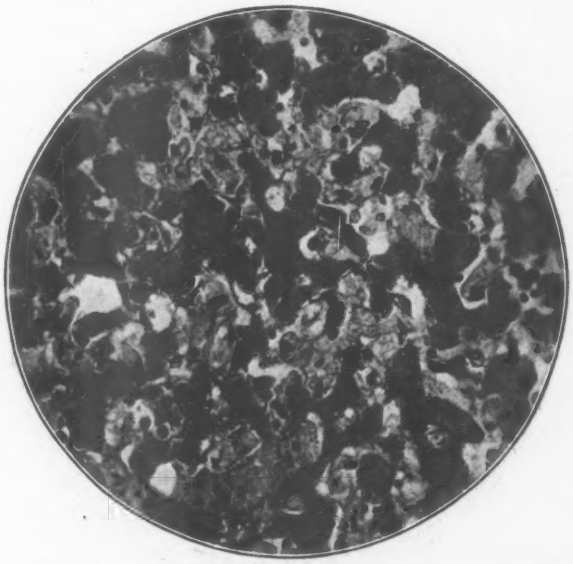

FIG. 2.—The centre of a liver lobule, showing a large number of endothelial cells lying between normal liver cells. (Photomicrograph × 250.)

Lymph Nodes. All of the nodes examined show the presence of a large number of endothelial cells, marked fibrous changes, and a great decrease or entire absence of adenoid tissue. The pigment is very abundant, confined, as a rule, to the sinuses bounded by the capsule and trabeculæ, and is crystalline in character for the most part. Chronic congestion is noted in all of the lymph nodes, but no hemorrhages are seen. Sections from the iliac nodes show by far the greatest amount of pigment as well as fibrosis, and almost complete absence of adenoid tissue. A careful study of the pigment in the iliac nodes shows that it is situated almost wholly in the endothelial cells throughout the entire node (Fig. 3). From one to four or five crystals are seen in each cell, the cytoplasm showing faintly

between the adjacent crystals. Wherever the cytoplasm is invisible, the pigment crystals are still arranged in a more or less circular form, showing that they are contained in, and limited by, a spherical body (Fig. 4). In these nodes the endothelial cells are undoubtedly acting as phagocytes.

Bone Marrow. The endothelial cells are much more numerous than in our earlier case; in fact, some sections show hardly any remnants of normal marrow tissue. Other sections present a few islands of marrow cells here and there. The endothelial cells are compressed and distorted, as a rule, and a delicate connective-tissue

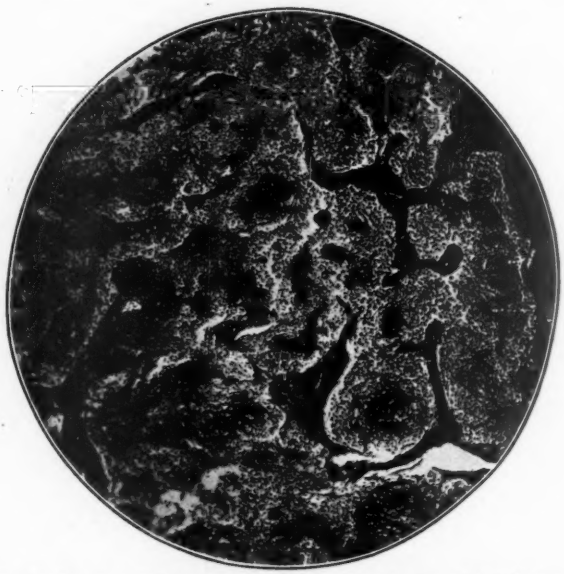

FIG. 3.—Section of an iliac lymph node, with complete absence of adenoid tissue. The entire section consists of connective-tissue reticulum and endothelial cells, the latter being filled with pigment crystals. (Photomicrograph × 45.)

reticulum is seen between them. A few large bloodvessels are present, also numerous capillaries. In one of the latter a distinct and typical endothelial cell is seen. The pigment is not abundant; when present, it is always situated in the immediate vicinity of the larger bloodvessels. The lesions in the other organs are not important, and have no bearing on the disease.

REMARKS. Since the publication of our first case, in March, 1905, two more cases of splenomegaly of the Gaucher type have been recorded. One case was demonstrated by Schlagenhaufer[3] at a

[3] Virch. Arch., 1907, clxxxvii, 125.

meeting of the German Pathological Society, September, 1906. The patient was a female, aged forty-one years, whose mother had suffered from tuberculosis thirty years ago. There were eight children, all of whom were healthy excepting one sister, who had an enlarged spleen. The patient had a "large abdomen" when five years of age, and at the age of twelve a large spleen was diagnosticated. Pigmentation of the face was noted nine years later. Examination of the blood showed hemoglobin, 65 per cent.; red cells, 4,700,000; leukocytes, 1300; the differential count was normal. Death was due to an acute cholangitis. Postmortem examination showed the following:

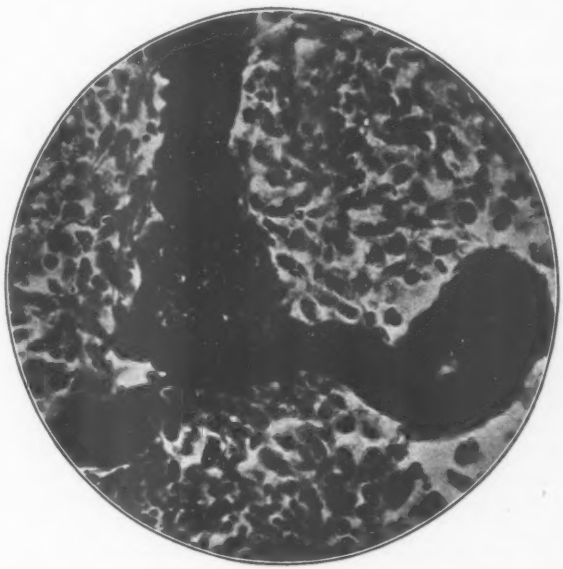

FIG. 4.—The same section shown in Fig. 3, showing the pigment crystals arranged in circular form or contained in endothelial cells. (Photomicrograph × 250.)

Skin of face and extremities yellow; face pigmented; icterus; right submaxillary glands enlarged and necrotic; no ascites. The spleen weighed 3510 grams, was of normal shape, reddish gray in color, and was studded with many nodules. The liver weighed 3000 grams. In the right lobe were multiple abscesses, in the left lobe several nodules. The mesenteric glands were large. The bone marrow was succulent in character and of a reddish color.

Microscopic examination of the spleen showed the usual picture found in the Gaucher type of splenomegaly. The pigment in certain situations, especially in the endothelial cells of the capillaries, did

not give the iron reaction, while the pigment surrounding the blood-vessels gave the usual reaction. Tests for amyloid and fat were negative. Cultures showed the colon bacillus. Smears made from the necrotic parts showed tubercle bacilli, but these could not be demonstrated in sections. Guinea-pigs inoculated with necrotic portions showed tuberculosis. Sections from the lymph nodes showed the typical picture of splenomegaly; the submaxillary nodes contained tubercles. The right lobe of the liver was the seat of acute cholangitis with multiple abscesses; tubercles were found in both lobes. The bone marrow presented the usual picture found in these cases, together with the presence of tubercles.

Schlagenhaufer believes that splenomegaly is a systemic disease analogous to lymphosarcoma, excepting that the reticulum is involved and not the cellular structures. Furthermore, he doubts the endothelial origin of the characteristic cells, and considers that they arise from proliferated reticulum. He also believes that tuberculosis may have an important bearing on the etiology of the disease.

In the discussion that followed the presentation of this case, Schridde was of the opinion that the cells are endothelial in nature, and called attention to the fact that such cells are found normally in the spleen and lymph nodes, but not in the marrow.

Sternberg believed that in certain individuals these cells might be present normally in the bone marrow, and if so, would then proliferate in the presence of this disease. Two years before, he had described a proliferation of these cells in the lymphatic hemapoietic apparatus occurring in certain forms of tuberculosis, and had noted these cells in the bone marrow. Sternberg also criticised the parallel drawn by Schlagenhaufer between splenomegaly and lymphosarcoma: (1) Because splenomegaly is undoubtedly a congenital disease, which lymphosarcoma is not; and (2) because lymphosarcoma shows malignant characters, in direct contrast to the course of splenomegaly.

The second case was reported by Marchand[4] in March, 1907. The patient was a woman whose age is not mentioned. A splenic tumor had existed for twenty years, and the liver was also enlarged. A tendency to hemorrhage was present; the skin was icteric and had a brownish color; no leukocytosis. Banti's disease was diagnosticated. At the autopsy the spleen weighed 2720 grams; the color was grayish red; scattered nodules were present, some of which were necrotic; no follicles could be seen. The liver was also enlarged (weight not given), and whitish streaks were noted between the lobules. The lymph nodes in the abdomen were enlarged and pigmented. The bone marrow was pale reddish gray and contained grayish white spots. Microscopic examination revealed the characteristic cells in the spleen, liver, lymph nodes, and bone marrow.

[4] Münch. med. Woch., 1907, liv, 1102.

Marchand examined these organs in the fresh state and calls attention to the peculiar homogeneous, glassy, or hyaline appearance of the cells, similar to amyloid. Sections treated with osmic acid gave no reaction for fat. He does not look upon the process as a simple hyperplasia of the protoplasm, but believes that some foreign substance of unknown nature has been produced in the cells. This substance, when treated with the ordinary reagents employed in histological methods, reacts in a peculiar manner, and causes the streaked and wrinkled appearance of the cells noted, together with the formation of vacuoles and granules. According to Marchand, these cells may arise either from the reticulum or from endothelium.

From a study of our own cases, and a review of those published by others, we can state the following:

Splenomegaly (Gaucher type) is a distinct disease, starting in early life, often affecting several members of a family, and running a chronic course. It may be recognized by a great enlargement of the spleen, which precedes a similar enlargement of the liver, and is unaccompanied by jaundice or ascites; by the discoloration of the skin, especially where exposed to light; and by the absence in the blood of any characteristic findings. The disease has none of the characteristics of malignancy, and usually terminates as the result of an intercurrent affection. The organs affected are the spleen, liver, lymph nodes, and bone marrow. Histologically these organs show the presence of large cells with small nuclei and a peculiar hyaline cytoplasm, which arise from the endothelium or normal reticulum, and the presence of pigment containing iron. The etiology is unknown, though a peculiar susceptibility of the endothelium or reticulum of the hemapoietic apparatus to some unknown toxic agent is most likely present. There is nothing in our cases even suggesting tuberculosis. We would say that when found in cases of this disease, it must be considered as a superimposed process.

PRIMARY CARCINOMA OF THE LUNGS.

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Primary carcinoma of the lungs, although not as rare as it is considered, and not as often diagnosticated as it might be, still warrants the reporting of every case that has been carefully studied both clinically and microscopically.

The author's patient was a male, aged sixty-four years, a German, and an insurance agent by occupation. Two of his brothers and one sister died of "galloping consumption," but no member of his

family had had carcinoma. His personal history was negative. He drank and smoked moderately and denied having had any venereal diseases. He had all the diseases of childhood, and at the age of twenty-eight, while in the army, he suffered from enteritis and had several attacks of acute articular rheumatism. He was admitted to the service of Dr. I. Adler at the German Hospital on November 18, 1906.

Up to a year previous to his admission he was perfectly well. After that his general health and strength began to fail. He lost 95 pounds in one year (formerly 245 pounds, now 150). Six weeks before admission he began to have severe cough, with very profuse mucopurulent expectoration; frequently his sputum was streaked with blood. He had very frequent night sweats, and often felt feverish. He had no chills, and never suffered from dyspnœa. He had no pain. His appetite was poor and his bowels were constipated.

On admission the patient was fairly well developed. The body was very much emaciated, the skin very dry. The eyes, ears, and nose were normal. The throat was red and inflamed. There was no glandular enlargement. The chest was broad and barrel-shaped; suprasternal, supraclavicular, and infraclavicular spaces were sunken. The right side above the fourth rib was considerably depressed, and amplitude of respiratory excursions was less than on left. There was normal tactile fremitus all over except at the right base posteriorly, where fremitus was absent. On percussion there was flatness on the right side posteriorly below the fifth dorsal spine, and hyper-resonance over the rest of the lung; on the left side there was slight hyper-resonance. On auscultation on the right side below the fifth spine there was very distant and diminished breathing sounds; egophony at level of the fifth spine; over the rest of lung exaggerated breathing. On the left side there was harsh vesicular breathing. This suggested a pleuritic effusion in the right chest. The heart was apparently normal in size, and there were no murmurs. The stomach was dilated; otherwise nothing abnormal was found in the abdominal cavity.

The extremities were normal. Rectal examination was negative. The prostate was not enlarged. The temperature during first days of admission varied between 99° to 100° in the morning, to about 101° to 103° in the evening. The pulse was 110 to 120; the respirations, 24 to 40. The urine contained a faint trace of albumin, had a specific gravity of 1011, and contained no casts and gave no diazo reaction. A blood count revealed: hemoglobin, 65 per cent.; red blood cells, 4,184,000; white blood cells, 12,600; polynuclears, 69.5 per cent.; lymphocytes, 28 per cent.; mononuclears and transitionals, 2 per cent.; eosinophiles, 0.5 per cent. No changes in red blood cells.

These data seemed to suggest a tuberculous pleurisy. The sputum, however, on repeated examination failed to show tubercle bacilli,

but always contained blood, white blood cells, and flat epithelial cells.

November 21. Two days after admission the right pleural cavity was tapped and about 150 c.c. of a bloody, slightly turbid fluid with specific gravity of 1025, was withdrawn, which on microscopic examination showed, besides numerous red blood cells, a slight predominance of polynuclear cells. Cultures of this fluid were sterile. The tapping did not very materially change the physical signs. Instead of absolute flatness, the percussion note was merely dull. The general condition of the patient was so far improved in that cough and expectoration were easier, but his respirations continued rapid.

November 29. Eight days after tapping, the flatness at the base of right lung reappeared, but with it were course crepitant rales, harsh breathing, and bronchial voice sounds, suggesting at the time a cavity in the lung separated from the chest by very thickened pleura. Sputum during this time was examined daily, but there was still no evidence of breaking down lung tissue. The patient continued with temperatures between 100° and 103° F., rapid respiration, cough, sweats, and pain in the right side of the chest until December 13 (three weeks after first tapping), when another exploratory puncture was made. With the needle in the seventh space posteriorly, and only after it was 6 cm. deep, was a thick brownish yellow pus obtained. Cultures were sterile. It was apparent now that we had either an abscess of the lung or, less likely, an encapsulated empyema to deal with. The general symptoms did not subside, so the patient was transferred to the surgical division.

On December 20 Dr. Willy Meyer resected the ninth rib, but found that pus came from a narrow channel above, and therefore resected the seventh rib. The abscess cavity was entered with the paquelin, and about four ounces of pus mixed with broken down tissue was obtained. The operator pronounced the cavity to be in the lung substance. The laboratory report of the tissue removed from the abscess was "lung tissue showing compression, congestion, œdema, and consolidation" (Dr. R. Weil). After this operation the high temperatures ceased, but the patient still had severe night sweats, cough, and expectoration. Repeated examination of the sputum showed no tubercle bacilli and no tumor cells, but constant presence of traces of blood. On and off the patient complained of slight pain in the right hypochondrium, but physical examination proved negative. Nothing new developed until

January 31 (six weeks after operation). Then the pains in the right hypochondrium became very severe, and the temperature rose to 104°. There was nothing new in the lungs or the wounds left from the operation to account for this, but just below the middle of the right costal margin in front, there was a distinct tender mass about the size of an orange, which moved with respiration. Fluctuation

was questionable. For several days the patient ran septic temperature, and a diagnosis of "empyema of the gall-bladder" was made. The high temperature gradually subsided.

February 15. Cholecystostomy was performed by Dr. Meyer. About a pint of pus and bile was evacuated and two gallstones, each about the size of a marble, were removed from the gall-bladder. From this operation the patient made an uneventful recovery, but the wounds in the chest healed slowly, the respirations remained accelerated, the temperature was about 100°, and there was still dulness and distant bronchial breathing at right base posteriorly. The patient became tired of hospital surroundings, so on April 1 (four and one-half months after admission) he left, but was to come to the outdoor department for dressing.

June 26. He returned to the hospital. He said that since he left he was able to be about, but he continued to have fever and his wounds in the chest were painful and did not heal. As before, he coughed and expectorated quite a good deal, and after each dressing he would spit up frothy blood. He had not lost much in weight and felt quite strong.

The condition of his lungs was essentially unchanged. There was dulness and rather peculiar distant harsh bronchial-like breathing at the right base posteriorly. The sinuses from the operation for abscess of the lung were not yet healed. Over the right scapula a baseball-like fluctuating mass was found. The axillary, occipital. and clavicular glands were not enlarged.

During his second stay at the hospital the symptoms were about the same as before. He coughed and sweat a great deal at night. Respirations were between 26 and 40, temperature ranged between 99° and 102°, and only occasionally did he complain of dyspnœa. The sputum was examined, but neither tubercle bacilli nor elastic fibres, nor any of the cells described as characteristic for neoplasm were found. Blood was always present.

July 23. The mass over the scapula, having become larger, was excised and found to be "carcinoma." From about this time the patient began to fail rapidly. His weight now was 123 pounds and dyspnœa increased.

September 5. While attempting to leave his bed, the patient collapsed and died from heart failure within five minutes.

The following are the notes of the autopsy performed several hours after death: The body is very much emaciated. Operation scar on the right and left sides of thorax posteriorly. Old scar over region of gall-bladder. Rigor not marked. Slight œdema of both lower extremities. No jaundice, no petechiæ, no glandular enlargement. Thorax cartilages of ribs completely ossified. Ribs break quite easily. The pleura on the right side reveals extensive adhesions below and posteriorly. On the left side there are firm adhesions posteriorly. Both sides contain several ounces of clear

serosanguinous fluid. The right leaf of the diaphragm is very much thickened (one-half to three-fourths inch), tightly adherent to the liver and the right lung. On section it has the consistency of cartilage and appears dense, white, and glistening. The left side is slightly thickened. The lower and middle lobes of the right lung are tightly bound together, forming one large, hard, solid mass. The pleural surface is very much thickened and presents two scars which dip downward into the underlying tissue. On section the lung cuts with marked resistance to knife, especially toward the hilum of the lung. On cut surface there is all along the outer margin of the lung a narrow strip (about one-half inch) which is all that remains of apparently normal lung substance. The rest of the lung is grayish white in color, granular, mottled here and there by darker areas, firm in consistency, and apparently made up of small nodules so closely packed together as to give an appearance somewhat similar to diffuse gray hepatization. The small bronchi are prominent. Their walls are thickened. Some have their lumens constricted, others are completely occluded. Few small bronchiectatic cavities varying in size from pea to lima bean are also observed, these being filled with yellowish creamy mucopurulent exudate. The upper lobe shows scattered irregularly throughout it many small, yellowish white, round areas about one-fourth to one inch in diameter, firm in consistency, circumscribed, and intimately associated with neighboring lung tissue. These areas do not have a cheesy appearance, and one cannot scrape any cheesy material from their cut surface. The rest of the lung shows slight congestion, œdema, and some areas of emphysema. At the apex of the left lung there are a few old calcareous tubercular foci and in lower lobe several metastatic nodules similar to those in the upper right lobe. The bronchial glands are very much enlarged, hard, closely adherent to larger bronchi, and on section present a diffuse grayish white appearance. The mediastinal glands are but very slightly enlarged. The supraclavicular and infraclavicular glands are not involved. The larynx, trachea, and bronchi are normal. The heart is dilated, the muscular coat very pale and flabby; there is marked calcific sclerosis of aortic and mitral valves and also of coronary arteries. The aorta contains many stone-hard round plaques and ulcerative areas. The œsophagus and thoracic duct are normal. The abdomen contains several ounces of clear serous fluid. Viscera in situ seem normal. Omental fat almost completely gone. The liver is enlarged and adherent throughout to diaphragm. Surface is irregular; scattered over it are few small, round, whitish nodules elevated above the surrounding liver substance and only slightly umbilicated. These are almost entirely on upper surface. At the falciform ligament there are many of these nodules grouped together, giving a mass about the size of a hen's egg. On section the liver cuts with resistance, and similar nodules are seen near the upper surface. The superficial nodules dip deeply into

the underlying liver substance. The rest of the liver is fatty. All that can be made out in the region of the gall-bladder is a thick fibrous scar. The spleen and pancreas are normal. The kidneys show moderate parenchymatous degeneration. The ureters, bladder, and genital organs are normal. The retroperitoneal glands are enlarged, but soft. The stomach is markedly dilated. The sigmoid flexure and rectum present small diverticula (about one-half inch in diameter) in communication with the intestinal lumen and following all along the line of the appendices epiploicæ. Vermiform appendix very large but normal.

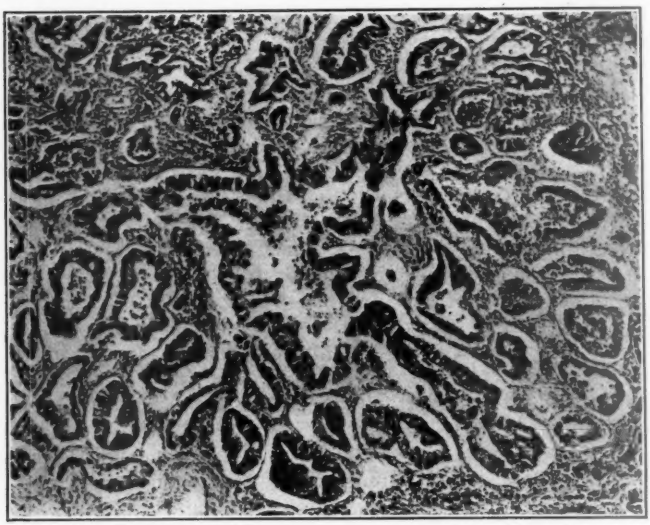

FIG. 1.—General alveolar appearance of the main tumor mass.

Anatomical Diagnosis: Primary carcinoma of the right lung, with secondary deposits in the left lung, bronchial glands, diaphragm, and liver.

The microscopic picture of the lungs is not uniform, but varies according as different parts of the lung or tumor are examined. Sections through the main mass of the newgrowth show alveolar structure (Figs. 1 and 2).[1] The alveoli are irregular in form and size, disorderly arranged, and indefinitely surrounded by a basement membrane. They are separated from one another by varying amounts of fibrous stroma with more or less round-cell infiltration. The lining cells are arranged in one and more layers, are not uniform in

[1] I wish to thank Dr. Leopold Jaches, of Cornell University, for his care in producing the photomicrographs.

size or shape, but more or less polygonal, and contain little granular protoplasm. The nuclei are large, and some of the cells contain more than one nucleus. Nucleoli are also seen. Very few of the alveoli contain mucus. Most of the lymph spaces and smaller bloodvessels are filled with these cells.

As the hilum pulmonis is approached the smaller bronchi, still containing cartilage, are found to be thickened, and in some places their mucous membrane is absent. The tumor process completely surrounds the bronchi, but here the newgrowth consists of large

FIG. 2.—Same as Fig. 1, but high power, showing the polygonal character of the cells.

strands or clusters of cells without a basement membrane and without any alveolar arrangement. Separating these islands of cells are bands of dense fibrous connective tissue. The cells are very large and irregular in shape, some polygonal, others round. The nuclei stain very deeply, are usually multiple, occupy almost the entire cell, and are in an active state of mitosis. Some of the lymph spaces are filled with these cells. These strands stretch forth and diffusely invade the surrounding lung substance. The malignant nature of this tissue is quite evident.

Within the bronchial walls are found the normal bronchial mucous glands, and scattered amidst these are nests of alveoli similar in appearance to those described within the main mass of the tumor. The mucous glands and these alveoli of neoplastic origin are strikingly different in their appearance, but in some sections an indisputable relationship can be traced in their histological structure. For example, close to a bronchial mucous gland there will be a larger alveolus also containing mucus, in part lined by a single layer of columnar mucus-secreting cells upon a basement membrane, but in the remaining part of the alveolus the mucous cells have disappeared and in their stead are found irregularly polygonal cells with larger

FIG. 3.—High power of bronchial wall. Within it is an alveolus lined in part by cells of a glandular-secreting character and in part by polygonal cells similar to those forming the tumor mass.

nuclei, heaping into several layers, and breaking through the basement membrane (Fig. 3). It is these polygonal cells which have been described above as constituting the main mass of the tumor. Such places of histological metamorphosis are not very numerous, but distinct and certain.

In the strip of lung tissue immediately adjoining the tumor and apparently normal in the gross, microscopically numerous air vesicles are found invaded by cancerous proliferation of the alveolar type. Here, however, we see a distinct basement membrane and a

single layer of columnar non-ciliated cells. Their protoplasm is homogeneous, somewhat translucent, and stains very faintly with hematoxylin. The nucleus is single, small, and situated toward the base. Most of the alveoli contain mucus. Bronchi are absent. This general structure is entirely different from any thus far described, and vividly suggests glands secreting mucus (Fig. 4).

The lung tissue not involved by neoplasm shows reactions of several kinds. The walls of the respiratory alveoli are almost all thickened. Many of these alveoli are in a state of consolidation

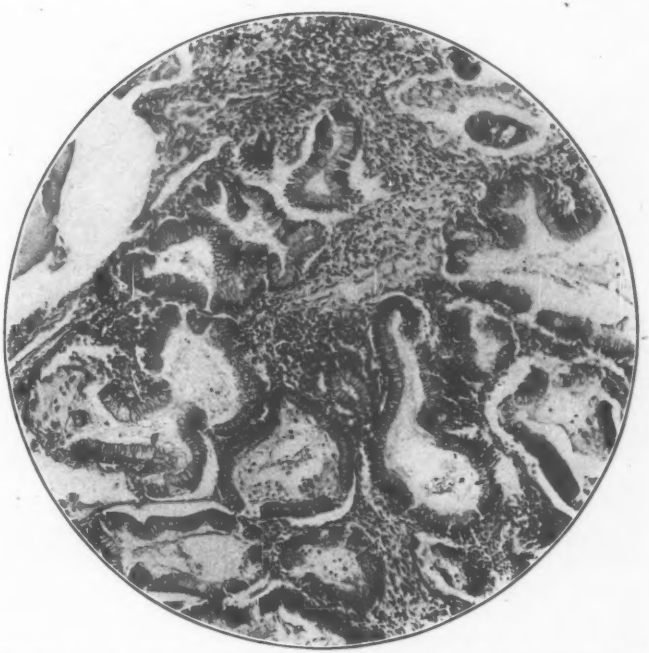

FIG. 4.—Section from macroscopically apparently normal lung tissue just outside of tumor mass. Shows alveoli of a distinctly glandular mucus-secreting type.

resembling pneumonia, the air vesicles being filled with fibrin, white blood cells, and desquamated epithelium. But the great majority show a catarrhal or desquamative inflammation, as they contain numerous swollen and degenerated epithelial lining cells. There are also areas of necrosis and areas with newgrowth of fibrous connective tissue infiltrated by leukocytes. Blood pigment is irregularly distributed within the tumor.

The metastatic nodules found throughout both lungs consist in part of the mucus-secreting glands, and in part of the alveoli lined

by polygonal cells. The nodules in the liver consist microscopically of strands of large, irregularly shaped, actively dividing cells with mitotic nuclei, and in some places attempting an alveolar arrangement but without regard whatever for the liver lobules (Fig. 5). The rest of the liver shows fatty degeneration and leukocytic infiltration. The type of tumor here is similar to that described above as surrounding the bronchioles. The bronchial glands, diaphragm, and subcutaneous tumor removed by operation show similar structure.

There seems to be no reasonable doubt that this is a primary cancer of the lung. The clearly metastatic nature of the nodules in the liver, diaphragm, bronchial glands, and left lung, and the absence

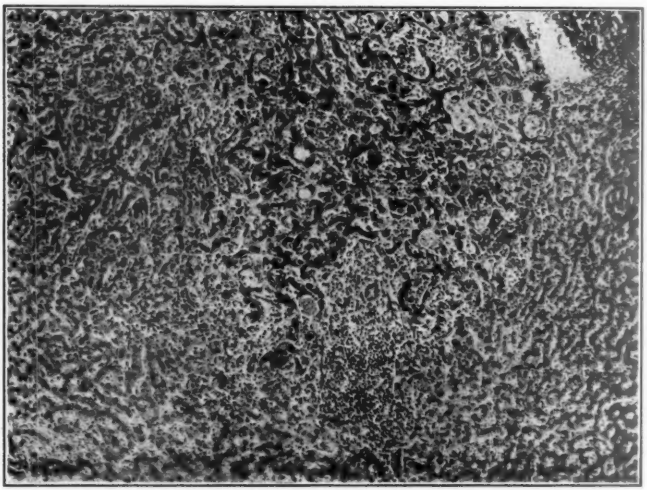

FIG. 5.—Liver with part of a metastatic nodule.

of tumor in every other organ of the body, furnishes convincing proof that the large tumor in the right lung is the primary seat of the cancer.

As to the starting point of primary cancer of the lung, we come to a subject of much discussion. Until comparatively recent times there was a tendency to fix upon the epithelium of the pulmonary alveoli as the point of origin of every lung tumor that was built up of polygonal or flat epithelium. At present it may be accepted as a fact that under varying conditions, mechanical and others, epithelium is very apt to change, and that the mere form of epithelium in the older and mature portions of the tumor can tell us nothing certain about its histological origin.

While the histogenesis of many cancers of the lung remains obscure,

it seems well assured that the great majority of this type of neoplasm is of bronchial origin, though carcinoma originating from the alveolar epithelium undoubtedly does occur. Those tumors that are of bronchial origin may start from the surface epithelium or they may take their origin from the bronchial mucous glands.

The tumor here described is of the latter class. For proof of this statement we must turn to those portions of the tumor which are the youngest and most recent in their development. These are clearly in our case those neoplastic foci scattered throughout the apparently normal lung in the gross, immediately adjoining the main tumor. The structure here is distinctly of a glandular mucus-secreting nature (Fig. 4). There is no part in the lung which this structure resembles more closely, or from which such a type of tissue can originate more readily, than from the bronchial mucous glands. Furthermore, the picture presented within the walls of the smaller bronchi still containing cartilage requires no hypothetical conclusions. Here we see distinctly the gradual development, from the epithelium of the bronchial mucous glands, of a new type of alveolus, lined by irregular polygonal cells. And it is this new type of alveolus which penetrates into the lung, fills the lymphatic spaces, invades the bloodvessels, and thus forms a great part of the newgrowth.

There are, no doubt, many portions of the neoplasm where, from mere examination of these parts only, one could not arrive at any definite results as to the origin of the tumor. Such places as the diffuse invasion surrounding the bronchial walls, the involvement of the diaphragm, and the metastases in the liver, belong to a stage of the tumor where it has lost its glandular mucus-secreting function and taken on, instead, the functions of growth and proliferation, and, therefore, appear differently. But here, too, one can trace a gradual transition between the earlier and later stages of this malignant growth.

From this summary, and the additional facts that the pulmonary alveoli and bronchial mucous membrane show no neoplastic tendency, there is conclusive evidence that this primary carcinoma of the lungs, originates from the mucous glands of the smaller bronchi still containing cartilage.

In completing this paper, there are several clinical features which presented themselves and which deserve a word of mention. As for the family history, our patient gave a distinct hereditary predisposition to tuberculosis. Several old tubercular lesions were found in the left apex. This co-existence of tuberculosis and carcinoma of the lungs, although denied in general by Rokitansky, is not at all rare. Wolff[2] has described 31 cases of carcinoma of the lungs, of which 23 were complicated by tuberculosis. Schwalbe[3] has described 10 cases, of which 3 were complicated by active tuberculosis. Further-

[2] Fortschr. der Med., 1895, Band xiii, No. 13.

[3] Deut. med. Woch., 1896, xii.

more Friedländer,[4] Hildebrand,[5] Seigert,[6] and Ribbert[7] described cases of carcinoma developing in tuberculous portions of the lung. These are only some of the references for the simultaneous occurrence of these two conditions.

In regard to the clinical diagnosis of tumor of the lung, this was made rather late in the disease. The probability of tuberculosis seemed so great that one was inclined at first to favor this diagnosis rather than carcinoma. The asymmetry of the chest, the diminished expansibility of the affected side, the bloody pleural fluid, and the persistence of dulness after evacuation of the fluid, can speak for both tuberculosis and carcinoma. The fact, however, that the apices remained practically clear while the process was localized entirely at the right base, and in addition to this the absence of tubercle bacilli, should have suggested strongly the diagnosis of carcinoma.

The sputum examination, too, proved interesting. It was examined almost daily, and the only almost constant finding was blood. Naturally it was profuse and mucopurulent. The variously described so-called characteristic "granule cells" ("Kernzellen") for carcinoma of the lungs were not found. As a rule, in a man over fifty, profuse expectoration which almost constantly contains blood and no tubercle bacilli, associated with physical signs denoting some abnormal lung condition, should always make one very suspicious of neoplasm.

The two complications which arose—the abscess of the lung and the empyema of gall-bladder—masked the diagnosis in the lungs to a great extent; but the fact that even after those operations the patient did not get any relief, but grew progressively worse, spoke highly in favor of an underlying malignant condition. When stenosis of the air passages became sufficient to produce symptoms, the diagnosis became more evident; but this, as usual, came late in the disease.

Summing up the age of the patient, the bloody pleural fluid, the persistence of dulness after tapping, and the constant presence of blood in the sputum without tubercle bacilli, one had enough ground for making the diagnosis of carcinoma of the lung.

I desire to express my thanks to Dr. I. Adler, through whose kind permission and help this case-report is published.

[4] Fortschr. der Med., 1885, No. 10, p. 307.
[5] Ziegler's Beiträge, 1888, Band ii.
[6] Virchow's Archiv, 1893, Band cxxxiv, p. 287.
[7] Deut. med. Woch., 1896, No. 11, p. 165.

THE DETECTION OF β-OXYBUTYRIC ACID IN THE URINE.

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In a considerable number of diseases, notably in diabetes mellitus, the detection of β-oxybutyric acid is of great interest and of importance both from a diagnostic and therapeutic standpoint. The statement, repeated in a number of text-books on chemical diagnosis, to the effect "that when a urine, which has been fermented, deviates the plane of polarized light to the left, the presence of β-oxybutyric acid may be inferred," is certainly hesitating enough to leave some doubt in our minds as to this mode of detection. This doubt is augmented when we review the list of substances at times found in the urine which may produce the same effect. Among those most frequently encountered may be mentioned creatinin and various compounds of glycuronic acid. Also certain compounds of lead, which are formed when lead acetate is added in the process of clearing urine for examination in the spectroscope, have been shown by Magnus-Levy[1] to possess a marked levorotatory action.

It is not for lack of methods for the detection of β-oxybutyric acid that I venture to suggest a new one. Procedures have been worked out by a large number of investigators—Tollens,[2] Wolpes,[3] Naunyn,[4] Stadelman,[5] Magnus-Levy,[6] Bergell,[7] Darmstäder,[8] Waldvogel,[9] Shaffer,[10] and Black.[11] Some of these methods are adapted to the quantitative as well as the qualitative determinations of β-oxybutyric acid, some of them have serious defects, practically all are laborious chemical procedures which require many hours of work, the facilities of a well-equipped laboratory, and the manipulations of a skilled chemist. Parenthetically it may be said that the methods recently proposed by Shaffer and by Black have added much to our facility in determining oxybutyric acid and appear to be very accurate.

The method which is here presented is exceedingly simple, requires little time, needs no elaborate chemical apparatus, and can be applied by any general practitioner. It depends upon the following principles: The removal of acetone and diacetic acid by heat, the oxidation of β-oxybutyric acid to acetone by means of hydrogen

[1] Arch. f. exp. Path. u. Pharm., 1899, Band xlii.
[2] Ann. d. chem., 1885, p. 228.
[3] Arch. f. exp. Path. u. Pharm., 1886, p. 21.
[4] Noth. Spec. Path. u. Ther., Band vii, 1, 181.
[5] Ueber den Einfluss de Alkalien auf d. mensch. Stoffer, Stuttgart, 1890.
[6] Arch. f. exp. Path. u. Pharm., 1901, Band xlv
[7] Ztschr. f. physiol. Chem., 1901, Band xxxiii.
[8] Ibid., 1903, i, 37.
[9] Die Acetonkorper, Stuttgart, 1903, p. 38.
[10] Jour. Biol. Chem., 1908, v, 211.
[11] Ibid., 1908, v, 207.

peroxide, and the detection of acetone in the urine thus treated by means of Lange's test.[12]

By boiling the preformed acetone, diacetic acid and the volatile fatty acids are removed from the urine; the boiling must be continued long enough completely to remove all of these bodies, and the urine after such treatment should give a negative result with Lange's test. This test depends upon the property of urine containing acetone to develop a purplish red color when treated with glacial acetic acid, a few drops of a watery solution of sodium nitroprussiate, and ammonia. The reaction is not given with alcohol or aldehyde; creatinin when present in considerable amounts gives a brownish color, which, however, may be distinguished from the purplish red color of the acetone reaction.

To the urine from which acetone, diacetic acid, and the volatile fatty acids have been removed, but which still retains its β-oxybutyric acid, peroxide of hydrogen is added. By this means the β-oxybutyric acid, as has been shown by Dakin,[13] is oxidized to acetone. It may be noted that this cannot be a quantitative method, even in a rough degree, since Dakin has shown that the end-products of the oxidation of β-oxybutyric acid by peroxide of hydrogen consist of different substances varying in amount according to the course which the oxidation process takes, and is never acetone alone.

An abbreviated outline of the chemical process involved may be represented by these formulæ:

$$\underset{\text{β-oxybutyric acid.}}{CH_3-CHOH-CH_2-COOH} + \underset{\text{Diacetic acid.}}{O=CH_3-CO-CH_2-COOH} + H_2O$$

$$\underset{\text{Diacetic acid.}}{CH_3-CO-CH_2-COOH} = \underset{\text{Acetone.}}{CH_3-CO-CH_3} + \underset{\text{Carbon dioxide.}}{CO_2}$$

In the course of a study of the acetone bodies extending over a number of years I have never found β-oxybutyric acid in the urine unless a strong Arnold's[14] reaction and a strong ferric chloride reaction (Gerhardt's) were present. To a urine showing these reactions the test for β-oxybutyric acid may be applied in the following manner:

To 20 c.c. of the suspected urine add 20 c.c. of water and a few drops of acetic acid and boil until the volume is reduced to about 10 c.c. To this residue add water to the original volume (*i. e.*, until it measures 20 c.c.). Put this into two test-tubes (B and C) of equal size, 10 c.c. in each test-tube. To one of the test-tubes (C) add one cubic centimeter of peroxide of hydrogen, warm gently for about one minute (do not boil), and then allow the fluid to cool. Add to each test-tube (B and C) one-half of one cubic centimeter of glacial acetic acid and a few drops of a freshly prepared watery solution of sodium nitroprussiate and mix. Overlay the solution in each test-

[12] Münch. med. Woch., 1906, Band liii, p. 1764.
[13] Jour. Biol. Chem., 1908, iv, 77.
[14] Archives of Internal Medicine, February, 1908.

tube with 2 c.c. of concentrated ammonium hydroxide. Allow these to stand for four or five hours, and at the end of this time compare the two test-tubes. At the point of contact between the ammonia and the underlying fluid B will show no ring (or a faint brown ring if much creatinin is present), test-tube C, to which hydrogen peroxide was added, will show a purplish red contact ring if β-oxybutyric acid was originally present; if β-oxybutyric acid was not present, the two test-tubes will not differ in appearance. If the two test-tubes are now shaken, the difference in color will be seen throughout the fluid; this difference is intensified by allowing the tubes to stand for fifteen or twenty minutes after shaking.

To detect slight differences in the color of the rings, the two test-tubes should be held side by side against a white background while the observer stands with his back to the light.

The oxidation by means of hydrogen peroxide is gradual and reaches its maximum in about four or five hours, after which the color slowly fades. When a very large amount of β-oxybutyric acid is present the difference in the two test-tubes may become evident in a few minutes. It is always well to prepare the two test tubes as above for comparison. B will show whether all preformed acetone and diacetic acid have been driven off, and will also show the creatinin ring (if present), so that its color may be compared with the color of the ring in tube C.

The test may be applied to the urine either before or after fermentation; the presence of sugar does not interfere with the reaction. If albumin is present it should be removed by filtration after the urine has been boiled.

The method is moderately delicate and will certainly detect β-oxybutyric acid when present to the extent of 0.3 per cent. and probably less.

The following table shows a number o urines in which the test, as above described, showed a positive reaction for β-oxybutyric acid in which the acid was quantitatively determined by Shaffer's method.

Specimen number.	Levorotation after fermentation.	Quantity in 24 hours, c.c.	β-oxybutyric acid.		
			Total grams.	Grams per liter.	Per cent.
1	0.7	4050	26.60	6.6	0.66
2	0.7	2310	11.94	5.2	0.52
3	0.5	1800	10.82	5.1	0.51
4	0.6	1800	9.15	5.0	0.50
5	0.5	4650	21.67	4.7	0.47
6	0.5	2550	8.01	3.1	0.31
7	0.2	3360	8.68	2.6	0.26

That the test is somewhat delicate may be inferred from the fact that I have obtained it in a number of diabetic urines with a levorotation after fermentation of 0.2 and a ferric chloride reaction much weaker than that given by any of the above urines in which the oxybutyric acid was quantitatively determined. It has been my experience that the amount of β-oxybutyric acid varies directly (although not necessarily proportionately) with the amount of diacetic acid present and that the ferric chloride reaction varies directly in intensity with the amount of diacetic acid present.[15]

In a number of normal urines tested the reaction has not been obtained. It was also absent in a number of urines showing a weak ferric chloride reaction.

THE EFFECT OF CERTAIN SO-CALLED MILK MODIFIERS ON THE GASTRIC DIGESTION OF INFANTS.

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In the fall of 1907, at the instigation of Dr. L. Emmett Holt, investigations were undertaken at the Rockefeller Institute in New York, in the hope of throwing light on some of the as yet obscure questions of infant digestion. The problem to be attacked was that of the digestion of milk in the infant's stomach, and more particularly the exact action of the more commonly used, so-called "milk modifiers," and their influence upon digestion both in health and disease.

A review of the literature of the gastric digestion of the infant[1] shows much valuable work on its physiology and its variations according to age and health. It has been shown that all the physiological factors occurring in the adult stomach are present in the infant, but in weaker form. It has further been proved that the younger the infant, the more active the motility of the stomach, that this motility is greater with woman's milk than with artificial food, and in health than in disease. It has been proved that the acidity of the gastric contents increases regularly after a meal for some time, but that free hydrochloric acid cannot be demonstrated for an hour or more after the ingestion of the food. This phenomenon has been shown to be due not to a lack of secretion of hydrochloric acid during the early stages of digestion, but to the striking power which

[15] Archives of Internal Medicine, February, 1908.
[1] Amer. Jour. Med. Sci., 1909, cxxxvii, 674.

casein has to combine with or adsorb it. Heubner has found that to 100 c.c. of cow's milk could be added 0.324 gram of hydrochloric acid before any test for the free acid could be obtained. Woman's milk will take up about one-half of that amount. It has further been proved that it is that hydrochloric acid which is combined with the protein which acts in peptic digestion, and that only, while the occurrence of free hydrochloric acid is merely a sign that more of the acid is present than is required for complete digestion of the protein. Opinions differ as to the occurrence of lactic and volatile fatty acids in the child's stomach, while the presence of a fat-splitting enzyme has been both asserted and denied. Pepsin is always found in the infant stomach in both health and disease, and gastric digestion goes on to the formation of small amounts of peptones but no amino-acids. Rennin is always present after the first few weeks of life. Whether before that, or not, is a moot question.

For many years the medical profession has been adding barley water and lime water to cows' milk to increase its digestibility, and in more recent years sodium citrate and malt extract have been used extensively. There are many physicians who believe that each of these substances is at times of value in infant feeding, and each probably has his own rules by which he determines which is indicated in a particular case. Such knowledge, however, is largely empirical, as we have but little idea, or, at least, proof of what these substances do in the stomach and what the chemistry of their action really is. With the exception of some work of Einhorn twenty years ago, in which he investigated the motility and acidity of the gastric contents after feeding woman's milk, cow's milk and water, cow's milk and barley water, and several artificial foods, practically nothing has been done along these lines.

In these investigations, it was considered advisable first to use normal infants. This, however, not being practical, owing to the difficulty of obtaining such in a hospital, children who approached as nearly as possible a normal state of health were selected. All were patients at the Babies' Hospital in New York, and none were suffering from obvious digestion disturbances at the time of the examination. To obviate, as far as possible, the error due to individual variations it was attempted to take each case through a complete series of comparative examinations. In all 122 observations were made on 24 such infants, varying from two to eight months of age.

The test feedings given were of three series, designated Series I, II, and III. The purpose of Series I was to investigate the effect of the substances employed upon gastric secretion and for this purpose they were given with water alone. The three test feedings of this series consisted of a 5 per cent. solution of milk sugar—as an inert substance—barley water, and a 5 per cent. solution of lime water. In Series II, the substance was added to a mixture of cow's milk and water, equal parts. In this series was included

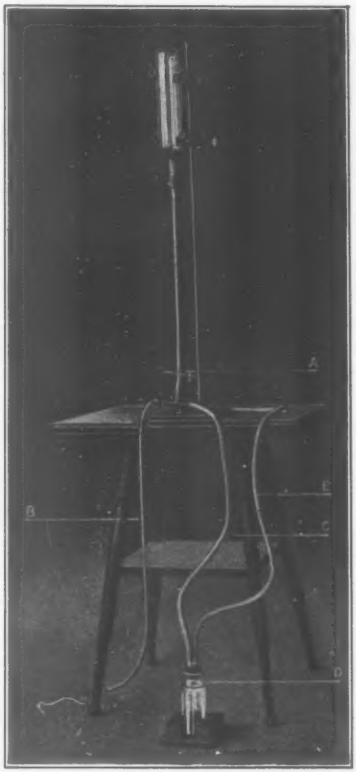
woman's milk undiluted. It therefore embraced woman's milk, cow's milk and water, cow's milk and barley water, equal parts, cow's milk and water with 5 per cent. lime water, and cow's milk and water with 1 grain of sodium citrate to the ounce. In Series III, experiments were made with cow's milk in the dilution of one part in four, and lime water, barley water and sodium citrate were investigated. In nearly all the cases, the test feeding was given the first thing in the morning, six to eight hours after the preceding nourishment. In a few only was the stomach washed a half-hour before the feeding. Owing to the various times which the child took in ingesting the meal, it was deemed more reliable to take the time from the minute at which the feeding was finished rather than from that of its beginning. This was done in every case.

On account of the difficulty sometimes encountered in removing the stomach contents of young infants by the ordinary method of stomach tube and funnel, and the necessity of working as rapiddly as possible, a special apparatus was constructed for this purpose (see illustration). This consists of a graduated glass reservoir holding 500 c.c. of water, attached by a clamp to an iron upright so that it stands about two feet above the table. From the outlet, two to three feet of soft rubber tubing leads to a T-tube of large caliber. Just above theT-tube is a pinch cock (*a*). Over one arm of the T-tube is drawn the stomach tube, a soft rectal tube either 22 or 23 French (*b*). From the second arm of the T-tube runs a stiff tubing (*c*) to a bottle on the floor (*d*). The bottle fits into a wooden stand to keep it in an upright position and is supplied with a tightly fitting rubber stopper, through which protrude two glass tubes. The tubing (*c*) from the T-tube fits tightly over one, while from the second extends about four feet of similar stiff tubing (*e*). This last is held in the mouth of the operator and is used to apply gentle suction when for any reason the stomach contents do not siphon quickly. The bottle is detachable and is used as a specimen bottle.

In the investigation under consideration, the contents were removed without washing. The rubber stopper was then transferred to a second specimen bottle and, when desired, the stomach washed by alternately opening and closing the pinch cock at the same time with the fingers pinching and opening the tube (*c*) from the T-tube to the specimen bottles. This wash water was not used for investigation, and the lavage was performed merely to make it certain that most of the stomach contents had been obtained, or for therapeutic purposes. It was surprising to see how large a stomach tube a young infant could be made to swallow if held in an upright position in the nurse's arms, if no attempt was made to pass the pharynx until the child took a deep inspiration. The tube was passed with great ease and apparently with a minimum of discomfort. Most of the children, after having overcome the initial fright, and having become slightly used to the procedure, made very little effort to cry

and some seemed quite content to suck on the tube. Though some of the babies failed to gain weight during the period of investigation —possibly due to the frequent changes in the foods used—no serious or injurious results followed the procedure.

The specimens were taken at once to the chemical laboratories of the Rockefeller Institute and under the supervision of Dr. P. A.



Apparatus used to evacuate the stomach. (For description see the text.)

Levene, submitted to the following examinations: The quantity was carefully measured in order that by this means a rough estimate of the gastric motility might be obtained (A)[2]. The inaccuracy of drawing exact conclusions owing to the varying consistency of the milk curd and the uncertainty of complete evacuation is thoroughly appreciated. The acidity was estimated by titration with $\frac{n}{10}$ NaOH,

[2] Letters in parentheses refer to the columns in the tables in which the results are recorded.

phenol-phthalein as an indicator (B). The hydrochloric acid in a free state was tested qualitatively with Congo red paper and quantitatively by titration against dimethylamidoazobenzol. The specimen used for the estimation of acidity, usually 5 c.c., after being neutralized was transferred to a platinum dish and evaporated over the steam bath to dryness. It was then carefully carbonized over a free flame, and the residue washed into a porcelain dish. In this, the chlorides were estimated by the method of Volhard. This result was calculated as parts per mille and recorded as "total chlorides" (C). A second portion of the contents was evaporated without the addition of NaOH, carbonized, and the chlorides estimated by the same method. This constituted the inorganic or fixed chlorides (D). The difference between the total chlorides and the sum of the fixed chlorides and free hydrochloric acid, shows the amount of chlorides which have gone into chemical combination with the milk proteins and are recorded as "organically bound chlorides" (E). It is this last item which is of importance in estimating the digestive capacity of various stomach contents when proteins are in the stomach. It has been shown by various authors that it is the combined chlorides only which act in peptic digestion, and that free hydrochloric acid in the stomach is merely a sign that more acid has been secreted than is required for complete digestion. The inorganic or fixed chlorides are, of course, inert. Acidity, fixed chlorides, and total chlorides will vary markedly with the food taken into the stomach, whereas the combined chlorides designate the exact amount which is being put to practical use. Tests were made in a number of cases for lactic acid, but as it was found in no case examined the proceeding was discontinued.

The method of estimating the digestive power of the gastric contents varied according to whether there were protein substances in the test meal or not. In Series I in which the "modifier" was given in water, without milk, the method was as follows: To each of the three portions of 5 c.c. of the contents was added 2 c.c. of fresh cow's milk. Portion A was untreated. To portion B was added $\frac{n}{10}$ HCl until the casein had become saturated with the acid, as shown by the test for free acid with Congo red paper. Portion C was boiled before the milk was added, and then acidified in the same way as D. To each portion was added 1 c.c. of toluol. For A and B 25 c.c. measuring flasks were used; C requiring boiling, was placed in a small Erlenmeyer flask. All these portions were then placed in the incubator at body temperature for twenty-four hours. At the end of this time C was washed into a 25 c.c. measuring flask, by means of a saturated solution of zinc sulphate in five per cent. H_2SO_4. Enough solid zinc sulphate was added to each flask to saturate the solution, and the contents then raised in volume to 25 c.c. by adding the saturated zinc sulphate solution. The flasks were then placed in the ice box for twenty-four hours more.

This latter proceeding was to insure a constant temperature at which the coagulation took place regardless of the season. At the end of the twenty-four hours the specimens were filtered through folded filter papers. The amount of N in 10 c.c. of the filtrate was determined by the Kjeldahl process. The amount of nitrogen calculated for the 25 c.c. is designated as "peptone nitrogen." The amount of N in the filtrate of portion C (I) that portion which was boiled previous to the addition of the milk shows the amount of peptone and residual N in the given amount of contents and milk, and is used as a control, the amount being subtracted from the amount of N in the filtrates of A and B.

The amount of N, theretore, in the filtrate of A after the deduction of C gives the absolute amount of N in the form of peptones which were produced by the action of 5 c.c. of the stomach contents upon 2 c.c. of milk in twenty-four hours (J), whereas the N in the filtrate of B, similarly corrected by the deduction of C, gives the amount of peptone formation in twenty-four hours when the amount of acid is practically the same in all cases—in other words, an estimate of the amount, or at least actively, of the pepsin itself (K).

In Series II and III in which milk was given in the test meal the procedure was somewhat different. The contents were thoroughly mixed and then three equal parts measured out: when possible 15 c.c. in each part, when lack of material prevented, 10 c.c. One portion A was saturated at once with $ZnSO_4$ and the volume raised to 25 c.c. by the saturated $ZnSO_4$ solution. The second portion B was placed in the incubator with toluol for twenty-four hours and then saturated with $ZnSO_4$, while the third portion C was acidified with $\frac{n}{10}$ HCl until the free acid showed a reaction to Congo paper, and then treated in the same manner as B. All three portions on being saturated with $ZnSO_4$ were placed in the ice box for twenty-four hours and then treated in a similar manner to the specimen in Series I. The amount of N in the filtrate of portion A represents the peptones and residual N in the stomach at the end of an hour (G). This is, however, but a very rough estimate of the gastric digestion which has taken place, as it is open to variations due to the amount of peptone in the food and to the much greater variation dependent upon absorbtion and motility. The difference, however, between the amount of peptone at the end of the hour and that of the twenty-four hours more in the thermostat, while not designating the digestion which has taken place, in the stomach may be used as an indication of the digestive power of the gastric juice at the time of its removal and is designated as "increase in peptone nitrogen" (J). The difference between the peptone N of C and A by eliminating variations in acidity similarly estimates the activity of the pepsin in the stomach at the end of the hour (K).

Lastly to each of three small test tubes was added 1 c.c. of gastric contents, in Series I unfiltered, in Series II and III filtered. Tube

I was untreated (L); II was acidfied with HCl until it showed bright red with dimethylamidoazobenzol (M); and III was boiled and acidfied (N). The digestive power of these were then tested by the method of Mette, the digestion being estimated after twenty-four hours at body temperature.

These results were of use not only to confirm the previous findings but to show the presence or absence of "free pepsin," that is, pepsin not combined with the protein. The absence in every case of albumen digestion in the specimen which had been boiled and acidfied (N) precluded the action of the acid in causing the digestion while the addition of toluol precluded bacteria.

Specimens of the test feedings as given to the patient were also examined for peptone N (Q), and total chlorides (P).

RESULTS. The results of these investigations are incorporated in tables of averages.

TABLE I.—*Normal infants. Investigation of lactose, lime water, and barley water administered in water, without milk. The specimen was removed from the stomach thirty minutes after the end of the feeding.*

	Number of cases	Amount of material removed from stomach	Total acidity	Total chlorides	Fixed chlorides	Free hydrochloric acid	Peptone nitrogen after 24 hours in the thermostat; untreated contents	Peptone nitrogen after 24 hours in the thermostat; acidified contents	Peptone nitrogen after 24 hours in the thermostat; boiled contents	Increase of peptone nitrogen; untreated contents	Increase of peptone nitrogen; acidified contents	Mette's tube tests; untreated contents	Mette's tube tests; acidified contents	Mette's tube tests; boiled contents
		c.c. A	% B	% C	% D	% F	mgr. G	mgr. H	mgr. I	mgr. J	mgr. K	mm. L	mm. M	mm. N
5% lactose solution	11	37	0.23	0.40	0.24	0.16	2.3	4.3	1.5	0.8	3.8	0.32	2.79	0
Lime water, 5 parts water, 95 parts Barley water	15	36	0.31	0.61	0.41	0.20	3.1	4.6	1.2	1.9	3.4	1.07	3.46	0
	12	50	0.34	0.82	0.69	0.13	2.6	5.4	1.3	1.3	4.1	0.35	3.00	0

Healthy Infants. Examining first Series I (Table I), in which the substance to be investigated was given with water only, the following facts will be noted: Using the sugar and water as a control, it is seen (A) that the amount of material obtained was smallest after sugar and water and lime-water, and larger after barley water. The total acidity (B) is higher after both lime water and barley water than after a plain milk sugar solution; the total chlorides (C) are higher after lime water than after sugar and highest of all after barley water; while the fixed or inorganic chlorides (D) vary in about the same ratio, leaving, however, most free HCl (F)

after lime water and least after barley water. From these results, it would appear that any increase in chlorides following the administration of barley water is due to the extra salt given in the food, while when the lime water is used, an absolute increase of hydrochloric acid secretion results.

Examining now the digestive power of the gastric juice, it will be seen (J) that 5 c.c. of the stomach contents was able to produce in twenty-four hours from 2 c.c. of cow's milk very little peptone after sugar, more after barley water, and most after lime water, while the next column, that in which the acidity was equalized to demonstrate the relative amount of pepsin (K), the variations are much less in proportion, but show, if anything, the greatest amount of pepsin after barley water. The Mette's tube experiment, when unacidified (L), confirms the relative digestive powers of the different contents (J), while the next column (M), the Mette's tube acidified, tends to show again that the amount of pepsin varies but slightly.

In Series II (Table II), that in which woman's milk undiluted and equal parts of milk and water were given in the test feeding, the amount obtained (A) after feeding woman's milk is distinctly higher than after the other feedings, which here include sodium citrate, one grain to the ounce. The total acidity (B) is practically the same in all cases though somewhat higher after each of the three "modifiers" than after the plain milk. The total chlorides (C) are again higher after barley water and lime water, but slightly lower after sodium citrate than after the plain milk. A marked variation appears in the fixed chlorides (D). Taking the milk and water as a standard, the fixed chlorides, after a feeding including lime water, barley water, and sodium citrate are distinctly raised. The increase after barley water is again explainable by the larger amount in the food (P), the other three feedings showing practically the same salt contents. The low total chlorides and fixed chlorides after woman's milk are also explicable from the smaller amount found in the food. There being in no case free HCl (F) found in these rich milk diets, the difference between the total and fixed chlorides was the active organically bound chlorides (E). This shows that, though after lime water a certain amount of the hydrochloric acid was converted into calcium chloride and rendered inert, nevertheless a sufficient excess of the acid was secreted to raise that organically combined with the casein to the normal and to fulfill the demands of digestion. After barley water, though the excess of chlorides was due in a large part to that given in the food, a slight increase of combined chlorides is shown. After sodium citrate, the sodium bound the greater part of the HCl, while no stimulation to a further increase was offered, thus leaving a minimum of acid to act in digestion.

TABLE II.—*Normal infants. Investigation of woman's milk and of lactose, barley water, and sodium citrate administered in equal parts of cow's milk and water. Time in stomach, sixty minutes after the end of the feeding.*

	Number of cases	Amount of mate rial removed from stomach	Total acidity	Total chlorides	Fixed chlorides	Organically bound chlorides	Free hydrochloric acid	"Peptone nitrogen" immediately	"Peptone nitrogen" after 24 hours in the thermostat; untreated specimen	"Peptone nitrogen" after 24 hours in the thermostat; acidified specimen	Increase in peptone nitrogen; untreated specimen	Increase in peptone nitrogen; acidified specimen	Mette's tube tests; untreated contents	Mette's tube tests; acidified contents	Mette's tube tests; boiled contents	Chlorides in the food	"Peptone nitrogen" in the food
		c.c.	‰	‰	‰	‰	‰	mgr. per 100 c.c.	mgr. per 100 c.c.	mgr. per 100 c.c.	mgr. per 100 c.c.	mgr. per 100 c.c.	mm.	mm.	mm.	‰	mgr. per 100 c.c.
		A	B	C	D	E	F	G	H	I	J	K	L	M	N	P	Q
Woman's milk, undiluted	5	100	0.97	0.88	0.37	0.51	0.00	53	81	104	28	51	0	1.08	0	0.20	41
Cow's milk and water, *āā*	13	52	0.84	1.12	0.72	0.39	0.01	27	68	98	41	71	0	2.39	0	0.46	16
Cow's milk and barley water, *āā*; 5% lime water	9	55	1.03	1.22	0.81	0.41	0.00	33	73	84	40	51	0	2.70	0	0.35	16
Cow's milk and barley water, *āā*	11	53	1.01	1.49	0.96	0.53	0.00	32	81	98	49	66	0	1.59	0	0.75	14
Cow's milk and water, *āā*; sodium citrate, 0.2%	8	55	1.03	0.98	0.89	0.09	0.00	25	65	86	40	61	0	2.40	0	0.41	13

A study of the amount of peptone N found in the stomach at the end of the hour (G) shows, with the exception of woman's milk, whose high content is due to the large amount of residual nitrogen in the food (Q), approximately similar results, with the lime water slightly the highest, and sodium citrate a shade low. The increase of peptone N during twenty-four hours in the incubator (J) shows that the digestive power following milk and water, lime water, barley water, and sodium citrate is about equal. The increase of peptone N after acidification with HCl and twenty-four hours in the thermostat (K) shows practically similar amounts of pepsin following cow's milk and water and cow's milk and barley water, whereas after sodium citrate and lime water it is a trace lower. This low figure after lime water is difficult to explain as it is at variance with all the other results. The amount of free pepsin, as shown by the Mette's tubes, is practically the same in all except woman's milk and barley water, which are low.

TABLE III.—*Normal cases. Investigation of lactose, barley water, and sodium citrate, administered in cow's milk, 1 part, water, 3 parts. Time in the stomach, sixty minutes after the end of the feeding.*

	Number of cases	Amount of material removed from stomach	Total acidity	Total chlorides	Fixed chlorides	Organically bound chlorides	Free hydrochloric acid	Mette's tube tests; untreated contents	Mette's tube tests; acidified contents	Mette's tube tests; boiled contents
		c.c. A	% B	% C	% D	% E	% F	mm. L	mm. M	mm. N
Cow's milk, 25% in water	7	36	0.75	1.33	0.64	0.65	0.04	0	2.66	0
Cow's milk, 25% in water, 5% lime water	7	30	0.97	1.27	0.60	0.64	0.03	0	2.50	0
Cow's milk, 25% in barley water	8	23	1.13	1.67	0.84	0.70	0.13	0	2.86	0
Cow's milk, 25% in water, sodium citrate, 0.2%	5	21	0.71	1.09	0.92	0.18	0.00	0	2.55	0

The third series of experiments as shown in Table III, that in which the substances under investigation were given with one part of milk in four, tend partially to confirm the findings of Series I and II. Lime water and barley water increase the total acidity (B), while the amount of free HCl (F) is too minute for consideration, though it should be noted that sodium citrate is the only substance used in this series, after which no free HCl was demonstrated in the gastric contents. The total chlorides (C) are highest after barley water and lowest after sodium citrate, while the fixed chlorides are highest after sodium citrate, leaving again an equality of combined chlorides (E) after milk and water and lime water and barley, with

a great decrease after sodium citrate. The figures demonstrating peptic digestion in this series are not very trustworthy, as the small amount of stomach contents usually obtained precluded thorough investigation of this point, and they are therefore omitted.

It would be inadvisable to attempt to draw definite conclusions from these series of experiments owing to the well known fallacies of averages in physiological work. A few facts, however, seem to be sufficiently suggestive to warrant their mention. It would appear, from the fact that in every case the addition of acid to the contents caused a greater increase of peptone formation than in the specimens in which the acid was not used, that when a deficiency of protein digestive power exists, it is due to a lack of acid rather than any want of pepsin. There is always more than enough pepsin in proportion to the amount of acid. As to the effects of the various substances investigated, it would appear that barley water has but slight, if any, effect upon HCl secretions. Lime water although usually given with the idea of reducing the acidity of the stomach may have quite the opposite result. Though a portion of the HCl found in the stomach is neutralized by the lime, the alkali stimulates to an increased secretion of HCl which may raise the acidity even higher than that obtained with milk alone. Sodium citrate, on the other hand, would appear to act in quite the opposite manner for, though preventing coarse curds, it converts most of the HCl into sodium chloride, liberating citric acid—a substance considered of little value in digestion—and does not stimulate further secretion of HCl. It would thus appear to weaken the protein digestive power of the gastric juice by using up its hydrochloric acid.

Pathological Cases. Having learned these facts concerning the physiology of the infant stomach and the effect of lime water, barley water, and sodium citrate upon the gastric secretion in health, it seemed advisable to undertake investigations upon cases suffering from digestive and nutritional disorders, in order to learn to what extent their gastric secretion varied from the normal and if possible to ascertain whether these various substances acted upon the diseased stomach in the same manner as upon the healthy organ. For this purpose two classes of cases were examined—marasmus cases without vomiting, and persistent chronic vomiting cases. Of the first class 14 cases were studied and 35 examinations were made, while of the chronic vomiting cases, 10 infants were used and 30 meals extracted. In these cases the test feeding given consisted of lactose, barley water, or lime water, given in water only, in the same concentration as was used with the healthy infants.

TABLE IV.—*Marasmus cases. Investigation of lactose, lime water, and barley water, administered in water without milk. Time in the stomach, thirty minutes after the end of the feeding.*

	Number of cases	Amount of material removed from stomach	Total acidity	Total chlorides	Fixed chlorides	Free hydrochloric acid	"Peptone nitrogen" after 24 hours in the thermostat; untreated contents	"Peptone nitrogen" after 24 hours in the thermostat; acidified contents	"Peptone nitrogen" after 24 hours in the thermostat; boiled contents	Increase of peptone nitrogen; untreated contents	Increase of peptone nitrogen; acidified contents	Mette's tube tests; untreated contents	Mette's tube tests; ac'dified contents	Mette's tube tests; boiled contents
		c.c. A	% B	% C	% D	% F	mgr. G	mgr. H	mgr. I	mgr. J	mgr. K	mm. L	mm. M	mm. N
5% lactose solution	14	20	0.28	0.34	0.21	0.13	3.5	5.7	1.6	1.9	4.1	0.22	3.62	0
Lime water, 5 parts; water, 95 parts	9	25	0.33	0.50	0.32	0.21	3.2	4.4	1.9	1.6	2.5	1.16	3.22	0
Barley water	8	30	0.40	1.46	1.19	0.20	3.4	5.0	1.7	1.7	3.3	1.33	3.84	0

TABLE V. (*Compiled from Tables I, IV, and VI*).—*Table showing the differences between the gastric contents of the various classes of infants studied. The test feedings consisting of a 5% solution of lactose in water. The stomach contents were removed thirty menutes after the end of the feeding.*

	Number of cases	Amount of material removed from stomach	Total acidity	Total chlorides	Fixed chlorides	Free hydrochloric acid	"Peptone nitrogen" after 24 hours in the thermostat; untreated contents	"Peptone nitrogen" after 24 hours in the thermostat; acidified contents	"Peptone nitrogen" after 24 hours in the thermostat; boiled contents	Increase of peptone nitrogen; untreated contents	Increase of peptone nitrogen; acidified contents	Mette's tube tests; untreated contents	Mette's tube tests; acidified contents	Mette's tube tests; boiled contents
		c.c. A	% B	% C	% D	% F	mgr. G	mgr. H	mgr. I	mgr. J	mgr. K	mm. L	mm. M	mm. N
Normal cases . .	11	37	0.23	0.40	0.24	0.16	2.3	4.3	1.5	0.8	3.8	0.32	2.79	0
Marasmus cases . .	14	20	0.28	0.34	0.21	0.13	3.5	5.7	1.6	1.9	4.1	0.22	3.62	0
Hypoacidity vomiting cases	4	40	0.15	0.19	0.09	0.08	2.3	3.9	1.7	0.6	2.2	0.08	3.50	0
Hyperacidity vomiting cases	6	28	0.44	0.52	0.20	0.33	4.5	6.9	2.1	2.4	4.8	1.61	4.55	0

The marasmus cases (Table IV) show very slight variation from the normal infants (Table V). The amount of material obtained

(the stomach was here evacuated thirty minutes after the child had finished its feeding) was slightly less than in the normal, whereas the total acidity and free HCl were practically equal in the two series. The increase chloride secretion following the administration of lime water shows quite as well in these cases as in the healthy children. It is of interest to note that the peptic activity in these cases is not reduced, appearing to be even a little greater than in the normal infants.

TABLE VI.—*Chronic vomiting cases. Investigation of the gastric contents in the two classes of this condition, and the effect of lactose, lime water, and barley water upon them. Time in stomach, thirty minutes after the end of the feeding*

	Number of cases	Amount of material removed from stomach	Total acidity	Total chlorides	Fixed chlorides	Free hydrochloric acid	"Peptone nitrogen" after 24 hours in the thermostat; untreated contents	"Peptone nitrogen" after 24 hours in thermostat; acidified contents	"Peptone nitrogen" after 24 hours in the thermostat; boiled contents	Increase of peptone nitrogen; untreated contents	Increase of peptone nitrogen; acidified contents	Mette's tube tests; untreated contents	Mette's tube tests; acidified contents	Mette's tube tests; boiled contents
		c.c. A	% B	% C	% D	% F	mgr. G	mgr. H	mgr. I	mgr. J	mgr. K	mm. L	mm. M	mm. N
Hypoacidity cases														
5% lactose solution	4	40	0.15	0.19	0.09	0.08	2.3	3.9	1.7	0.6	2.2	0.08	3.50	0
5% lime water solution	3	34	0.06	0.40	0.37	0.01	1.6	3.8	1.2	0.4	2.6	0.00	3.20	0
Barley water	2	33	0.27	0.55	0.42	0.06	3.5	4.3	1.9	1.6	2.4	0.00	4.42	0
Hyperacidity cases														
5% lactose salution	6	28	0.44	0.52	0.20	0.33	4.5	6.9	2.1	2.4	4.8	1.61	4.55	0
5% lime water solution	6	23	0.39	0.60	0.30	0.31	3.2	4.4	1.7	1.5	2.7	1.05	3.52	0
Barley water	4	38	0.39	0.77	0.54	0.21	3.2	4.2	2.1	1.1	2.1	0.59	3.58	0

In the *chronic vomiting cases* (Table VI), of which ten were studied, it was early seen that they naturally fell into two classes. In four of them the acid contents was distinctly subnormal and in the other six it was exceptionally high. In the *hypoacidity vomiting cases* the total acidity (B) was very slight and free HCl (F) either absent or present only in minute traces. These cases responded slightly to the administration of lime water, as is shown by the higher total chloride content of the stomach, but not sufficiently to neutralize the lime, and the free HCl was present in a trace only in one case. The peptone-forming power of the untreated stomach contents was somewhat low, while the action on the Mette's tubes was practically nil (L). That the failure of digestive power was due to a lack of acid,

and not to any deficiency of pepsin is shown by the strong action in the Mette's tubes after acidification of the specimens (M).

In the *hyperacidity vomiting cases* (Table VI) the total acidity (B) and free HCl (F) were distinctly high after all the test diets, the total chlorides and fixed chlorides varying in the same ratio as in the normal. The peptone formation from milk was also distinctly above normal (J) as was the Mette's tube estimations. The lack of an increase of digestive power of the acidified specimen, with the single exception of the milk sugar specimens, shows that this increase of proteolysis is again due to an increased acidity and not to any increase of pepsin.

Finally to learn whether these effects of the salts used in infant feeding occurred in all cases, a short series of experiments were made in which 18 unselected infants, the entire content of a ward, were examined for the acidity and chlorides (Table VII). In these cases the test feeding consisted of two parts of cow's milk and one part of water, and the substances used were lime water, 5 per cent., sodium citrate 0.2 per cent., and potassium carbonate 0.1 per cent., with sufficient lactose to make the carbohydrates 6 per cent. The meals were extracted one hour after the child received the bottle, in this respect differing from the other experiments. In this series the effect of lime water shown in the other experiments is not evident, but that of sodium citrate is fully confirmed by the increase of the fixed chlorides and consequent reduction in the organically combined chlorine. The potassium carbonate also increased the fixed chlorides and reduced the organic chlorine, but not so markedly as did the citrate. There was no increased stimulation of HCl by this salt.

TABLE VII.—*Unselected ill infants. Investigation of sodium citrate, lime water, and potassium carbonate administered in a mixture consisting of cow's milk, 1 part, water, 2 parts, and lactose sufficient to make 6%.* (1.40–6–1.30.)

	Number of cases	Amount of material removed from stomach	Total acidity	Total chlorides	Fixed chlorides	Organically bound chlorides	Free hydrochloric acid
		c.c. A	‰ B	‰ C	‰ D	‰ E	‰ F
Cow's milk and water . . .	18	46	0.85	0.98	0.29	0.69	0
Cow's milk and water; 5% lime water solution	17	51	0.78	0.94	0.24	0.68	0
Cows milk and water; sodium citrate 0.2%	13	44	0.85	0.91	0.65	0.26	0
Cow's milk and water; potassium carbonate 0.1%	15	52	0.64	0.97	0.44	0.52	0

REVIEW OF RESULTS. While fully appreciating the danger of drawing definite conclusions from the results of physiological investigations when these results are based on averages of the findings, a review of the above tables would seem to suggest at least certain facts. The motility of the stomach appears to be in inverse proportion to the concentration of the milk in the solution. The greater the dilution the more rapidly the organ empties itself. Lime water itself appears not to act, as is generally accepted in practical pediatrics, by reducing the acidity of the child's stomach. While unquestionably neutralizing a portion of the hydrochloric acid, the alkali stimulates in a further secretion of gastric juice. This raises the amount available in the form of free acid or organically bound chlorine at least to the amount normally occurring when the lime water is not added, and may cause a distinct over-stimulation of the gastric glands sufficient to produce a slight relative hyperchlorhydria. The effect of barley water in the stomach appears, at least from the purely chemical viewpoint, to be very slight, neither stimulating nor retarding gastric secretion. The action of sodium citrate, however, is quite definite. It acts similarly to the alkalies in converting a large portion of the hydrochloric acid into sodium chloride, while at the same time it does not stimulate to a further secretion of acid. In this way it reduces decidedly the amount of hydrochloric acid in the stomach. How potent a factor this may be in the well known action of this salt in preventing the formation of curd in the infant stomach is an open question. It has been shown by several observers that in the young infant the amount of rennin is very slight and it is possible that most of the clotting is due rather to the action of the acid in the stomach than to the ferment.[3]

[3] That sodium citrate does act in inhibiting acid clotting is shown by the following simple experiment: Into each of eight Erlenmeyer flasks was placed 5 c.c. of fresh cow's milk and varying amounts of *n*/10 sodium citrate solution. After sufficient distilled water had been added to make the volume of fluid the same in all the flasks the solutions were titrated with *n*/10 HCl until clotting occurred. From the accompanying table it will be seen that each increase in the sodium citrate in the milk required a proportional increase of the HCl to produce the clot.

Flask	Cow's milk c.c.	*n*/10 sodium citrate added to milk c.c.	Distilled water added c.c.	Amount of *n*/10 HCl required for clotting c.c.	Increase in the quantity of HCl required for each increase of 1 c.c. sodium citrate c.c.
1	5	0	7	2.0	—
2	5	1	6	2.3	0.3
3	5	2	5	2.6	0.3
4	5	3	4	2.85	0.25
5	5	4	3	3.2	0.3
6	5	5	2	3.45	0.25
7	5	6	1	4.00	0.55
8	5	7	0	4.30	0.3

An examination of the individual cases treated with milk mixtures containing sodium citrate showed that in those cases in which the acidity of the stomach was low practically all the hydrochloric acid was converted into sodium chloride, while in those of high acidity

Protein digestion in the stomach of the young infant would appear to be very slight and such as does occur to be in fairly direct proportion to the amount of acid present.

PRACTICAL APPLICATION. A practical application of these results is suggested in connection with the class of infants who vomit persistently from birth. According to these results these cases, while showing no especial clinical differences, may be divided into two fairly definite groups according to the acidity of their gastric contents. If the hyperacidity found in the majority of these cases is the chief cause of their vomiting the fact of the excess of acid and its degree should be known in order that the treatment may have a rational basis. The administration and removal of a test feeding in a young infant is a simple procedure, the greatest difficulty being the finding of the most appropriate substance to be used. A simple five per cent. solution of lactose in water has shown the most striking differences between the acid content of the stomach of individual infants and appears to be the most suitable feeding to test the gastric contents. It might, however, be well to follow this test after a day by a second examination in which a mixture of cow's milk, one part to water two parts is used. By this means the stomach both in comparative rest and during active digestion may be studied and the amount of acid actually secreted, owing to the stimulation of the milk, determined. It seems probable that the results of such findings will give some important indication for treatment. When the acidity is low, a weak alkali to stimulate acid secretion or possibly a few drops of dilute hydrochloric acid will be indicated, whereas if an oversecretion of hydrochloric acid is found, either a higher protein meal, thereby binding more of the acid, or sodium citrate to convert the hydrochloric acid into sodium chloride may be found effective. The accurate knowledge of the degree of acidity may be of especial value in cases of congenital pyloric stenosis or pylorospasm. In the one case we have had the opportunity to examine, the gastric acidity was exceptionally high. This agrees with the findings of Knoepfelmacher, Engel, and others. If, as seems probable, the pylorospasm is due to the hyperacidity, an accurate knowledge of its degree must be of no little value in treatment.

SUMMARY. 1. The motility of the infant stomach varies inversely to the concentration of the food. The more dilute the food the more frequently may the feedings be given.

2. Lime water does not reduce the acidity of the gastric contents, the neutralizing of a portion of the acid being overcome by an

the amount of the fixed chlorides was increased by a fairly definite amount, namely 0.043 per cent. A calculation of the amount of hydrochloric acid which should theoretically combine with 0.2 per cent. sodium citrate shows that one would expect 0.061 per cent. Allowing for the increased dilution from the gastric juice it would seem that the 0.043 would approach rather nearly the theoretical amount and that, therefore, the combination of HCl with sodium citrate in the stomach closely follows chemical laws.

increased stimulation of hydrochloric acid by the gastric glands. This may even increase the amount of acid available for digestion.

3. Sodium citrate acts on the acid in the stomach converting it into sodium chloride and thus markedly reduces the "available hydrochloric acid."

4. Barley water seems to have no constant effect upon the chemistry of gastric digestion in the infant.

5. The type of infants who vomit persistently may be divided into two classes, hypoacidity and hyperacidity.

6. Test feedings should be given to this type of infants to determine to which class they belong.

7. A five per cent. milk sugar solution seems to be the most satisfactory feeding to determine fine differences in the gastric contents. This may be followed by a mixture of milk one part, water two parts, to determine to what extent the gastric glands are capable of responding to stimuli. For the lactose solution thirty minutes is the most satisfactory time to allow the feeding to remain in the stomach; for the milk mixture sixty minutes.

8. On purely theoretical grounds it would appear that when the acidity is low either small doses of alkalies or of hydrychloric acid are indicated while in hyperacidity sodium citrate holds out the best hope of benefit.

9. Protein digestion in the infant's stomach is slight and is proportional to the amount of hydrochloric acid in the organ.

I desire to express my thanks to Dr. L. Emmett Holt for the inspiration and the many valuable clinical suggestions given during the course of this work; to Dr. P. A. Levene for his aid in directing and overseeing the chemical side of the problem; and to Dr. Hemenway, resident physician, her assistants, and the nurses of the Babies' Hospital for their coöperation and kind assistance.

BOILS: A NOTE ON THEIR TREATMENT.[1]

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Not long ago ringworm was regarded as a constitutional disease, and rules were given as to the general treatment of the patient in order to effect a cure. This ancient tradition still lingers, in so far as some doctors still insist that ringworm of the scalp is more obstinate in strumous than in other patients, and in them constitutional

[1] Read at a meeting of the Alumni Association of the City (Charity) Hospital, New York, January 13, 1909.

treatment is important, if not essential, for its cure. There is no doubt that ringworm is a purely local infection by some form of the trichophyton, and has nothing whatever to do with constitutional states. As the trichophyton is a vegetable fungus, it will grow better in some soils than in others, and so some people are more susceptible than others to infection by it. What the peculiar condition of the soil is we do not know. We do know that at the age of puberty some change takes place in the scalp that renders it no longer a proper soil for the growth of the trichophyton, and a ringworm that has long been on the scalp disappears even without treatment. We also know that ringworm is practically never seen on the scalp of an adult.

Boils, likewise, have nothing to do with constitutional states, but are due to local infection with staphylococci. We see them breaking out as small epidemics at times. Some rowing crew composed of young men in superb physical condition develops such an epidemic. One of their number contracts a boil on his hand, and others of them get boils from handling the oars. Surely here is no vice of constitution, but a pure infection. Boils are most often seen on the back of the neck. Surely there is no constitutional condition conceivable that would cause them to limit themselves to that region. They appear there simply because the back of the neck is subject to slight traumatism, as from the rubbing of a rough collar or a collar button, and this gives the chance for the pus organisms to find entrance into the skin. Boils are frequently seen in diabetes, in which there is a grave constitutional disorder. But they are seen frequently also in scabies, in which there is no question of a constitutional disorder. In both instances their presence is due to the slight traumatisms of the skin caused by the scratching to relieve the itching, and the consequent opportunity for the entrance of the pus organisms.

It need not surprise us that boils are as frequent as they are. The surprise is that they are not more frequent than they are, the special fungus being so common that it is often found on damp cloths hung up in a room. The only explanation of their comparative infrequency is that, as in ringworm of the scalp, there is some peculiarity of the tissues of some individuals that makes them more susceptible to infection, while the majority of individuals are protected by an absence of such peculiarity.

Perhaps it may be asked: "How about crops of boils of which we hear so much?" Crops of boils are due most always to bad treatment of the first boil. When a boil developed from the infection of a skin follicle, the old and classic method was, and is, to poultice the boil, and when it came to a head, or "pointed," to open it with a crucial incision, squeeze out the pus, and replace the poultice. When we consider that a boil is due to a vegetable fungus somewhat like the yeast plant, how could we do better to cause it to grow

luxuriantly than to supply it with heat and moisture? And if we desired to produce a crop of boils, how could we do better than to smear the warm, moist surface with a pure culture of the fungus, as we do when we squeeze the pus over the surface of the skin after opening the boil?

Again, we meet with cases in which boils appear on different parts of the body. This condition is called furunculosis. It does not mean that there is any constitutional infection, but simply a transference of the common infection from one part to another by the fingers, or something else, in a person who is susceptible to the infection. It is true that this form of boils occurs at times in persons who are in poor general health, who on that account have their resistance to infection lowered. But still the sole cause of the boils is the local infection.

For a quarter of a century I have treated all boils, no matter where located, according to the method taught me by my friend Dr. George H. Fox. Scores of such cases have been treated by me both in public and private practice with uniform success. Though I have gone over the literature of the subject, I have found no mention of the method. As it is simple, safe, and effective, no excuse is necessary for making it the subject of this communication.

For the treatment of boils all that is necessary is a small piece of stick sharpened to a fine point, a little absorbent cotton, a 95 per cent. solution of carbolic acid, and a 5 or 10 per cent. ointment of salicylic acid. As soon as the boil has pointed, and it has usually done so when the patient comes to us, a small bit of the cotton is wound about the pointed stick, dipped in the carbolic acid, and bored into the softened point of the boil. This gives a chance for the pus to escape and thoroughly disinfects the cavity of the boil. The boil is not to be squeezed. The surface of the skin in the neighborhood of the boil is then washed over with peroxide of hydrogen, or a solution of bichloride of mercury, 1 in 1000, and the salicylic acid ointment spread on old washed cotton or linen cloth, or several thicknesses of gauze, laid over the boil and the adjacent region. That is the end of that boil, as a rule. If it is a very large boil, the operation may have to be repeated the next day. The ointment is to be kept constantly on the affected part for a week. Of course, a few new boils may appear for a few days in the region, the result of the infection of the skin follicles before this treatment was instituted. They are to be treated in the same way, and a cure will soon be attained.

If a patient comes to us before the boil has pointed it may be aborted by injecting into it a drop or two of a 5 to 10 per cent. solution of carbolic acid, or touching its top with 95 per cent. carbolic acid, while the above-mentioned salicylic acid ointment is used as a dressing.

There is no question that warm poulticing will relieve the pain of a boil, because it relieves tension of the skin. If such a dressing is thought to be necessary there is no harm in using compresses of hot boric acid solution. It is not necessary if the boil is punctured with pure carbolic acid, because the acid produces anesthesia in a few moments. Many times have I seen patients who have been kept awake for nights by the throbbing pain of the boil, go home and sleep quietly after the carbolic acid has been used.

As cases illustrative of the results of the treatment here advocated I would cite the following:

CASE I.—Man, aged forty years. Ten days before I saw him a boil appeared. He had poulticed it, and a second boil had formed. I injected three drops of 10 per cent. solution of carbolic acid into the new boil, and bored into the old one with pure carbolic acid. Over all a 10 per cent. ointment of carbolic acid was placed. Prompt and complete recovery.

CASE II.—Girl, aged nine years. She had a boil the size of a small cherry over her right eye. It was swabbed out with pure carbolic acid and covered with a 5 per cent. ointment of salicylic acid. Prompt and complete recovery.

CASE III.—Woman, aged sixty years, For about three years she had had a succession of boils about her head and neck. The above treatment was used. She made a prompt and complete recovery, and had no new boils for eight months, when I lost track of her.

CASE IV.—Man, aged forty years. He had had a series of boils for four months. After they had been treated as above he made a prompt and complete recovery.

CASE V.—Man, aged eighteen years. He had his first attack of boils one year before he came to me. It lasted under the old method of treatment for three or four months. Three weeks before he came to me the boils had begun to appear. Under the above treatment he promptly recovered.

CASE VI.—Man, aged forty-eight years. He had had a boil on the end of his nose for three weeks, which had been lanced. One application of the carbolic acid followed by the salicylic acid ointment ended the trouble in a few days.

CASE VII.—Man, aged thirty-seven years. He had had a series of boils on the back of his neck and hands for fifteen months. He had them lanced, dressed with bichloride solution, poulticed, and had taken yeast and many kinds of medicine from many physicians. When I told him he would be well in three or four weeks without taking any medicine, he laughed at me. In two weeks all the boils had disappeared. One month afterward one small one came, which also became well under one application of the acid. Nine months after, he came to me at my request and reported that he had had no more boils.

It will be noted that in all these cases not one drop of medicine was given by the mouth. I commend this treatment, asking that it be tried, and being sure that one will be convinced of its efficacy. It has one not small advantage over the usual surgical plan of incision, which is that it leaves a hardly appreciable scar. Thus, the patient escapes bearing a cross on the back of his neck for the rest of his life and advertising the fact that he once had a boil.

Opsonins and vaccines now occupy the centre of the medical stage. I do not deny their value, and in an extensive case of furunculosis I would use them. But in the usual run of cases what is the use of going to the trouble and expense of using them, when such excellent results can be obtained by using a pointed piece of wood, a minute amount of absorbent cotton, a drop of 95 per cent. carbolic acid, and a few cents worth of salicylic acid ointment?

REVIEWS.

MEDICAL GYNECOLOGY. By HOWARD A. KELLY, A.B., M.D., LL.D., F.R.C.S., Professor of Gynecological Surgery in the Johns Hopkins University, Baltimore. Pp. 662; 163 illustrations. New York and London: D. Appleton & Co., 1908.

"IT will be my effort in the following pages to review my special field, in an endeavor to return to the general practitioner that portion of it which he ought to recover by right of his prior lien." This quotation from the preface of the volume before us gives its keynote. Some will feel, we believe, that the author has tried to return more than is wise, but be that as it may, he has produced a most valuable book which fills a long left want. His first chapter of forty pages is devoted to the consideration of the various methods of conducting the gynecological examination, together with a consideration of some of the more common symptoms. In this connection he takes occasion distinctly to place himself on record as opposed to indiscriminate operative correction of uterine displacements for the relief of backache by the epigrammatic statement that, "from backache to uterus in women and backache to kidneys in men is a fallacious mode of reasoning." We are also glad to call attention to his belief that, as a rule, coccygeal operations are failures from the standpoint of the relief of pain. On the other hand, we are sorry to note his dictum that the operation for the repair of the lacerated cervix is generally a most useless procedure. The two following chapters upon the hygiene of infancy and girlhood, and normal menstruation and the menopause are most excellent, and the former is particularly to be recommended to the perusal of all physicians bearing the responsibility of family practice. The consideration of dysmenorrhœa is, in the main, all that could be desired, although we fail to see why the author has included in his treatment the use of the intra-uterine electrical applications. Admitting that this may be a permissible therapeutic agent to the trained specialist, we must strongly deprecate its use by the men for whom this book was specifically prepared. Neither do we believe that it is advisable that the general practitioner be encouraged to perform the "simple" operation of cervical dilatation and curettage of the uterus. The training necessary to the proper selection of cases suitable for the procedure, together with the necessity for surgical cleanliness, removes this operation from

the domain of medical practice. The chapter upon intermenstrual pain, together with those upon amenorrhœa, menorrhagia, and metrorrhagia, are most satisfactory, and his statement that, in the treatment of hemorrhage in young or unmarried women, the use of douches and local treatments is "gynecological tinkering" would form a good motto for many an office even at the present day; its observance, we fear, would considerably deplete the income of some of our brethren. We are delighted to see that in his consideration of the treatment of extra-uterine pregnancy there is no place given to the "waiting policy." The consideration of the general subject of constipation is most careful and thorough, and will well repay careful study, since it must be admitted that much bad advice is prevalent. Those of us who have passed through the period when active post-operative purgation was considered an essential will be most enthusiastic in regard to the mild measures enjoined by the author for the treatment during this trying time, particularly if we have had any actual knowledge in our own person of the more heroic earlier methods.

In his especially pleasing chapter upon backward displacements of the uterus it is a pleasure to find that that valuable little instrument, the pessary, receives adequate and respectful treatment. The statement that the so-called Alexander operation is gradually going out of fashion among gynecologists will be questioned in some quarters. The chapters upon pelvic inflammatory disease, sterility, gonorrhœal infection, and syphilis are as valuable as the extended experience of the author would lead one to expect. To the last mentioned subject he has devoted fifty pages. This, in a book of this nature is remarkable, but very praiseworthy, since among general practitioners there is a lamentable lack of practical knowledge upon all phases of this subject, except the general appearance of the primary lesion in the male, and the dose of protoiodide. Chapters upon abortion and the injuries and ailments following labor are replete with interest, and it is needless to state that the advice given is sound, although we feel that there is a good deal of ground to conclude that the operation of curettage of the partly emptied uterus is as much the operation for the specially trained man, we do not say the specialist, as are any of the simpler abdominal operations. The chapters upon fibroid tumors and carcinoma are complete presentations from the non-operative standpoint, and the emphasis placed upon the need for the education of women in the matter of the importance of early medical attention in all suspicious cases is to be especially praised. The limit of operative interference has been reached, it would seem, and any betterment in operative results depends upon the diagnostic ability of the general practitioner and the dissemination of knowledge among women. There may be some question as to the proper method, but no intelligent physician can escape the conviction that the laity should be trained to recog-

nize the early symptoms of this disease. In the chapter upon cystitis the author gives in detail the method used by himself in cystoscopic examinations of the bladder. We know that Dr. Kelly is most expert in the use of the instrument that bears his name, but we doubt whether it is feasible to expect that anyone who does not make a practice of examination of the bladder can in the occasional case expect to get any results by the use of the instrument advocated. We moreover doubt very decidedly whether anything but harm would result by the adoption of the cystoscope as a part of the office armamentarium of the general practitioner. In any event, we feel from personal experience that for inspection of the bladder and catheterization of the ureters, one of the electric instruments with water distention will give better results after a much less tedious training. The chapter upon the functional nervous diseases most commonly seen by the gynecologist is a much needed chapter. The author is to be congratulated that it has been included. The volume concludes with chapters upon appendicitis in its relation to disease of the pelvic organs, splanchnoptosis and movable kidney, and post-operative conditions. In brief, the book is a most thorough and satisfactory exposition of non-operative gynecology, written from the standpoint of actual personal experience. It should be not only in the library of every general practitioner, but should be carefully read from cover to cover. W. R. N.

BIER'S HYPEREMIC TREATMENT IN SURGERY, MEDICINE, AND THE SPECIALTIES. By WILLY MEYER, M.D., Professor of Surgery in the New York Post-Graduate Medical School and Hospital, and PROFESSOR DR. VICTOR SCHMIEDEN, Assistant to Professor Bier in the University of Berlin, Germany. Pp. 209; 95 illustrations. Philadelphia: W. B. Saunders Company, 1908.

THIS manual was written by the authors in order to supply a demand apparent to them for a brief and comprehensive description of the hyperemic treatment that would enable the surgeon, specialist, and general practitioner to become familiar with the method. The term "Stauungshyperämie" is taken over from the German language because the authors failed to find any word in English which would exactly cover the principle of the procedure. They object to the usual terms stasis, obstructive, congestive, induced, passive hyperemia, etc., as expressing but poorly the cause and physiological effect. The advantages of the method are well known, and it has been exploited for the last few years in many publications by Bier and his pupils. The book comprises the methods of induced hyperemia, general rules for its application and

its clinical use in surgery, medicine, gynecology, obstetrics, otology, ophthalmology, rhinology, pharyngology, laryngology, neurology, psychiatry, and dermatology. From this formidable list, which embraces nearly every condition that can be imagined, with the exception of certain infectious diseases, it will be seen that despite the statement of the authors that hyperemia is not to be considered a panacea, the wide range of diseases in which it is recommended will make it seem so, especially to the superficial observer. The methods of application are lucidly described, the illustrations are clear and descriptive, and the indications generally are well defined, but it does seem as though such an undercurrent of enthusiasm governs the statements of the authors as to cause some doubt of their claims. It need only be mentioned that the method is recommended in the treatment of cerebrospinal and spinal meningitis, diphtheria, burns, and even in cases of inoperable sarcoma and carcinoma to realize the extent to which enthusiasm will carry an advocate of a treatment which has a special action. As to the book itself, there is little to say except in commendation, although more attention might have been given to the theory of the method.

G. P. M.

PROGRESSIVE MEDICINE. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College, assisted by H. R. M. LANDIS, M.D., Demonstrator of Clinical Medicine in the Jefferson Medical College, Philadelphia. Vol. I, 1909, pp. 277. Philadelphia and New York: Lea and Febiger, 1909.

THE first volume of *Progressive Medicine* for this year begins with an excellent critical discussion, amounting to 114 pages, of recent progress in the surgery of the head, neck, and thorax, by Charles H. Frazier. Special attention has been devoted to cerebral trauma, cranial defects in epilepsy, brain tumors, hydrocephalus, abscess of the brain, the cranial nerves, diseases of the jaw, carcinoma of the lip, torticollis, Ludwig's angina, glandular enlargements and tumors of the neck, disorders of the thyroid gland, including exophthalmic goitre, diseases of the parathyroid glands, diseases of the œsophagus, diseases (especially tumors) of the mammary gland, empyema, bronchoscopy, the surgery of the heart, and a wide range of other diseases. Robert B. Preble devotes 52 pages to infectious diseases, including epidemic disorders and the relationship thereto of milk infection, cerebrospinal fever, diphtheria, dysentery, influenza,

malaria, the plague, pneumonia, rheumatism, scarlet fever, typhoid fever, etc. Floyd M. Crandall devotes 31 pages to recent progress in diseases of children, discussing especially the mortality rate in infants, ophthalmia neonatorum, congenital laryngeal stridor, arthritis, rickets, dentition, recurrent vomiting, and feeding. D. Braden Kyle discusses rhinology and laryngology, particularly recent progress in atrophic rhinitis, nasal obstruction and irregularities of the teeth and palate, diseases of the accessory sinuses, intracranial diseases of nasal origin, foul breath, adenoids, diseases of the tonsils, stuttering, tracheotomy, etc. Arthur B. Duel discusses diseases of the ear, especially suppurative labyrinthitis, brain abscess, the surgery of the facial nerve, cholesteatoma, the mastoid operation and its after-treatment, and the changes in hearing that occur in advanced life. The volume, as a whole, well fulfils the intentions of the editors, and may be commended as a virtual necessity to the practitioner who desires to keep abreast of the progress of medicine. A. K.

A GUIDE TO THE CLINICAL EXAMINATION AND TREATMENT OF SICK CHILDREN. Second edition, greatly enlarged and rewritten. By JOHN THOMSON, M.D., Physician to the Royal Edinburgh Hospital for Sick Children, Joint Clinical Lecturer on the Diseases of Children, University of Edinburgh. Pp. 629; 160 illustrations. Chicago: W. T. Keener & Co., 1909.

THIS second edition of Dr. John Thomson's well-known *Guide*, which originally appeared in 1898, has been amplified to a size more than twice that of the original, and now appears as an imposing volume, beautifully printed and embellished with a profusion of half-tone illustrations. Founded upon a series of lectures delivered to classes of students and graduates attending the author's clinics at the Royal Edinburgh Hospital for Sick Children, the subject has been approached purely from a clinical standpoint, and thus the personal inspiration of the teacher can be traced clearly throughout the text, lending a touch of authority that serves to emphasize the salient facts and rivet the reader's attention. Differing thus from the construction of the usual text-book on diagnosis, the plan of the work adopts a more natural method of reasoning from the symptomatology as presented to the student who approaches a case as a problem and must work out his diagnosis from a comprehensive study of its clinical features. Appropriate stress is repeatedly laid upon the importance of using the eye in the clinical investigation of children's diseases, an art that is too apt to be neglected at the present day, when laboratory investigation can be so easily called upon for outside help.

Especial commendation must be given for the chapters on the diseases of the nervous system and of the digestive organs, which are unusually complete and are further illuminated by striking photographs of the facies of these diseases. Altogether this new edition offers a most helpful guide to the practitioner and student whose opportunities for the study of disease have been less extensive among children than among adult patients. It can be commended also as especially safe and temperate in its therapeutics, which reflects the seasoned experience of one of the most accomplished and widely known of British medical writers on pediatrics. T. S. W.

RETINITIS PIGMENTOSA, WITH AN ANALYSIS OF SEVENTEEN CASES OCCURRING IN DEAF MUTES. Being an Essay for which was awarded the Alvarenga Prize of the College of Physicians of Philadelphia, 1908. By WILLIAM T. SHOEMAKER, M.D., of Philadelphia. With Laboratory Examinations of the Blood and Urine by JOHN M. SWAN, M.D., of Philadelphia. 10 illustrations and three colored plates. Philadelphia: J. B. Lippincott Co., 1909.

THIS is an admirable essay, and with it and Nettleship's elaborate communication on Retinitis Pigmentosa and Allied Diseases, recently published, the reader is in possession of the fullest information on this interesting subject. Dr. Shoemaker has analyzed the extensive and often conflicting literature in such a way as to present briefly its best conclusions. He has added in an important manner to this literature by the record of seventeen cases of retinitis pigmentosa occurring in deaf mutes, and, with the aid of Dr. John M. Swan, has included the results of an investigation of the metabolism of the subjects of this disease which he himself has studied. The chapter on etiology is particularly good, and the interesting discussion on heredity and consanguinity in their relation to this disease is a good example of how much information can be given in a few well written paragraphs. Dr. Shoemaker concludes that heredity is a potent etiological factor, that parental consanguinity is of importance only in connection with heredity and environment, and that syphilis as a true cause of retinitis pigmentosa has not been established. He calls attention to the carelessness of the reports of many cases, and how frequently real retinitis pigmentosa and various types of pigmented chorioretinitis have been confused. He is in accord with the majority of observers that this disease is not an inflammation, and therefore deprecates the use of the term "retinitis pigmentosa," which, as he expresses it, should give way to the term "degen-

eration" or "sclerosis." While the laboratory investigations, which include thorough analysis of the blood and urine of the seventeen cases constituting the basis of this essay, made by Dr. Swan in the laboratory of physiological chemistry of the University of Pennsylvania, are most interesting, they have thrown no light on the nature of the disease, and, as Dr. Swan says, have been of no assistance in establishing its etiology or diagnosis. Dr. Shoemaker is much to be congratulated upon this essay, which is well worthy of the prize it received. G. E. DE S.

HUMAN FOODS. By HARRY SNYDER, B.S., Professor of Agricultural Chemistry in the University of Minnesota. Pp. 362; 76 illustrations. New York: The Macmillan Co., 1908.

WRITTEN as a text-book for students who have taken a course in general chemistry, this book will be scarcely likely to find a place in the library of the physician. For those wishing a closer insight into the chemistry of foodstuffs and the changes these undergo during cooking and digestion, the volume may be of benefit; but as an aid to dietetics, or for use in general medicine, it will prove of little value. The author's style is clear, and even to those not acquainted with general chemistry the subject is readily intelligible. Some of the illustrations seem unnecessary, since a great many are unaccompanied by any explanatory note. For instance, Fig. 3 shows an apparatus for the determination of fat; but without a word of description the cut is meaningless, except to laboratory workers, and the picture of a flour mill (Fig. 39) serves no purpose and offers no illustration of the text. Criticism may be made of the author's failure to make use of the metric system, since this system is in general use in scientific work. Thus, on page 11 he says, "a pound (of starch) yields 1860 calories;" and in other places the Fahrenheit scale is used instead of the centigrade. Temperatures should be expressed in terms of both systems. To the laity, for whom this book is also written, the interchangeability of "proteid" and "protein" is most confusing; and since the latter word has been recommended by American physiologists and chemists, its use is to be preferred. The index is far from satisfactory, as not only is there no attempt at an alphabetical arrangement of subjects, but there are important omissions; for example, no reference is given to tyrotoxicon, which is described on page 85. With more careful attention to proofreading (on page 21 the author says, "One part of nitrogen is equivalent to 5.25 parts of protein," instead of 6.25), judicious elimination of some of the cuts and text, and a revision of the index, the book will be of value to those for whom it is especially written —students of agricultural chemistry. E. H. G.

VENOMS, VENOMOUS ANIMALS, AND ANTIVENOMOUS SERUM THERAPEUTICS. By A. CALMETTE, M.D., Corresponding Member of the French Institute and of the Academy of Medicine, Director of the Pasteur Institute, Lille, France. Translated by F. E. AUSTEN, F.Z.S. Pp. 403; 125 illustrations. New York: William Wood & Co., 1908.

FOR fifteen years Calmette has carried on investigations upon the physiological action of venoms, and during this time a great number of papers have been published from his laboratory upon this subject. It seemed, therefore, advisable to collect these observations and summarize the results in book form. The entire question, however, is considered in the form of a treatise and the general literature upon the subject is fully utilized. The book, of some 400 pages, is divided into five parts, each containing several chapters. Part I is of an introductory nature and deals with the classification, habits, and detailed descriptions of the poisonous snakes. Part II is concerned with the chemical and physiological action of snake venoms. It is as one might suppose, one of the longest sections in the book, covering about 100 pages. In these chapters, the experiments which have lead up to the explanations of the poisonous action of the venoms upon the organs of the body and the blood, and the bacteriolytic and enzymotic properties of venoms are considered in a clear and satisfactory manner. This part and the following one on the antevenomous serum therapeutics is the section of the book which contains most of the results of the important investigations which have been made within recent years, for the remainder of the work is more or less concerned with zoölogical questions. Part IV, however, is very interesting and is devoted to a discussion of the venoms in invertebrates, fishes, and mammals. In these chapters many interesting facts are collected, and since the literature upon the subject is given in some detail, it forms a very valuable section. The book concludes with three "documents," which are in reality a series of case histories upon the treatment by antivenomous serum of human beings and domestic animals bitten by poisonous snakes. Besides the purely scientific discussions there are numerous short accounts of such subjects as the immunity of animals to snake bites and descriptions of the methods used by snake charmers in India and elsewhere. The book is fully illustrated and well translated.

W. T. L.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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A Clinical Method for the Serum Diagnosis of Syphilis.—NOGUCHI (*Münch. med Woch.*, 1909, lvi, 494) refers to the complexity of the Wassermann reaction and the practical impossibility of obtaining satisfactory results from it unless it is carried out by an experienced worker. A well-equipped laboratory is essential. Therefore the method cannot be applied as generally as would be desirable. The author has simplified the procedure and has attempted to devise a method which can be used by the general practitioner. He finds that filter paper may be impregnated with antigen and with serum which is hemolytic for human red corpuscles. A third paper may be prepared for the free complement, though it is safer to obtain this fresh from guinea-pig serum. By cutting the paper into pieces of appropriate size, the required amount of antigen, hemolytic serum, etc., is obtained. The technique of the method is given in detail and must be rigidly adhered to. In a series of two hundred cases parallel experiments with the original Wassermann technique and the new method showed the latter to be slightly more delicate.

The Mercurial Reaction as an Element of Diagnosis in Syphilis.—CURIONI (*Lancet*, 1908, ii, 1810) has made a study of the urine of syphilitic patients for the identification of mercury. He gave the patients 0.01 of perchloride of mercury hypodermically at 11 A.M. and examined the urine eight, fourteen, and twenty hours later. A positive mercurial reaction is the finding of mercury in the urine by the method of Vitali, namely, the isolation of the mercury by copper filings and the production with iodine of the yellow or the red iodide of mercury. In studying 30 syphilitic patients

and 20 non-syphilitic, he discovered that the elimination of mercury in the urine of the syphilitic is always much slower than in the case of the healthy individual. He found the reaction absent in cases of recent syphilis showing symptoms, and only a slight reaction, never so evident as in normals, in individuals in whom two or three years have elapsed since the primary sore. Finally, long-standing cases (ten to twelve years) of syphilis give as positive a reaction as normals. He explains the phenomenon by the hypothesis of the formation of a combination of the mercury and the syphilitic virus which does not readily pass through the renal filter. The combination results in the destruction of the virus. He has not applied the test to tabes and general paresis, but believes they will excrete mercury as readily as do normal individuals. He recommends the test to be of service in doubtful cases of syphilis for practitioners who are not trained to the more complicated technique of the Wassermann reaction.

Demonstration of the Trichinella Spiralis in the Circulating Blood in Man.—Herrick and Janeway (*Arch. Int. Med.*, 1909, iii, 263) have confirmed the prediction of Staübli that the application of his method to man would result in its becoming a ready means of diagnosis of trichiniasis. His method consists in laking the blood from a finger puncture with 3 per cent. acetic acid, and examining the centrifugalized sediment for the embryos. They were able to study the disease in a mother and seven daughters, in all of whom the diagnosis was made by the clinical findings of nausea, vomiting, diarrhœa, muscle pain, œdema of the eyelids, and the demonstration of an eosinophilia. In two instances trichinellæ were found with apparent ease in the laked blood of the mother. Herrick and Janeway lay stress upon this as the final proof of the distribution of Trichinella spiralis by way of the blood stream. They believe examination of the feces practically fruitless as a means of diagnosis, and hope this method of Staübli will prove a more ready and less painful diagnostic method than the excision of muscle.

Mitral Stenosis and Congenital Malformations.—J. Heitz and A. Lézary (*Arch. d. mal. d. cœur, d. vaisseaux, et d. sang*, 1908, i, 701) call attention to the frequent association of mitral stenosis and various disturbances in mental and physical development. They agree with those authors who believe that this co-existence is proof of a congenital origin dependent upon some toxic or infectious cause, and they point out the need of demonstrating such arrested or anomalous physical developments as would date back to intra-uterine life. They emphasize the need of searching for such causes as syphilis, tuberculosis, or alcoholism in the parents. Only about fifteen cases in the literature fill these requirements; the malformations in these cases include imbecility, syndactylia (Dumolard), harelip (Marie), asymmetry of the base of the brain, ectopic testicles, and sternal malformations. To these cases they add two which have come under their own observations. The first was a man, aged forty-eight years, who had a pure mitral stenosis and a hemihypertrophy, involving the left arm and leg, which they considered traceable to intra-uterine life. The second, a better case, was a young man, aged seventeen years, an imbecile, with small testicles, a bifide uvula, and an anomaly in the union of the two rami of the lower jaw.

At the symphysis there was a median depression between two longitudinal ridges of bone. In the heart were the signs of a pure mitral stenosis. Neither of these patients had ever been ill. No other possible etiological element was apparent. However, no toxic or infectious cause was discovered in their parents. Two autopsies performed upon patients having mitral stenosis and congenital malformations seem to favor fœtal endocarditis rather than arrested development in the production of the valvular lesion. In Faure's case the valve was thickened and indurated, with welding of the leaflets and hypertrophy of the chordæ tendineæ. Klippel and Clerc's case showed a slightly thickened valve and a patch of sclerosis. Heitz and Lézary interpret these thickenings and sclerosis as undoubted cicatrices of an old inflammation. Such an intra-uterine infection could be the cause of both the mitral stenosis and the arrested or anomalous development in the cases described.

Tuberculous Endocarditis.—DEGANELLO (*Il Policlinico*, December, 1908) reports the results of his attempts to produce a true endocarditis in rabbits by inoculation of the anterior chamber of the eye with tubercle bacilli after mechanical and chemical injury of the endocardium. In no instance was he successful. Nor did the intravenous injection of a mixture of tubercle bacilli and powdered charcoal cause inflammatory changes in either the parietal or valvular endocardium. He recalls the fact that Marchiafava, in a large series of autopsies upon tuberculous subjects, has never observed specific lesions of the endocardium. However, Landouzy and Gougerot (*Presse médicale*, 1908, xvi, 761) were able to produce a generalized tuberculosis in guinea-pigs by the inoculation of fragments of the injured valves from two cases of endocarditis in infants. In the first case the endocarditis was secondary to a pulmonary tuberculosis; in the second, it was a primary septicemia. The lesions upon the valves consisted of mononuclear, fibrinous inflamamations. No bacilli had been found in the sections.

Observations on Experimentally Induced Choked Disk.—CUSHING AND BORDLEY (*Johns Hopkins Hospital Bulletin*, 1909, xx, 95) state that their experience with over 400 cases of choked disks is in favor of a mechanical explanation of this condition rather than a toxic or inflammatory one. Their clinical observations have shown them (1) evidences of stasis in the eye grounds leading rapidly to a measurable œdema of the nerve head in cases of trauma, cerebral apoplexy, and simple cerebral œdema from concussion or contusion. In these cases the cause cannot be anything else but the mechanical influence of increased intracranial tension, operative relief of which leads to prompt subsidence of the congestion and œdema of the disk. (2) They believe that the condition of the eye grounds in cases of brain tumor and of nephritis is of a common origin, pressure, which in the latter case results from cerebral œdema. (3) They have seen a great number of instances of partial or total subsidence of choked disk after simple decompression, which more than any other factor, favors a mechanical rather than a toxic source of the neuroretinal change. By a series of experiments upon dogs they show that a neuroretinal œdema with marked elevation of the papilla accompany conditions which raise intracranial pressure whether from the introduction of new fluid under tension or from transmission

of tension to the fluid already present; and further, that a visible distention of the optic sheath occurs probably antecedent to the production of the neuroretinal change. Simple stasis in the retinal veins fails to produce anything more than the venous engorgement which accompanies a choked disk. It does not lead to a definite œdema of the papilla, the latter apparently requiring the concomitant action of fluid under tension in the optic sheath. They find that long continued pressure against a dural defect can lead to retinal hemorrhages and other clinical, as well as histological, features which characterize chronic choked disk in man. In conclusion, they state: (1) That the occurrence of the neuroretinal œdema is primarily dependent upon the passage of cerebrospinal fluid under tension from the subarachnoid spaces of the interpeduncular region into the vaginal sheath of the optic nerve, and that cerebral decompression often allows the process to subside, owing to a resultant diminution of tension from release of confined fluid. (2) That their experimental work corroborates many more recent clinical observations in showing that a choked disk, even of considerable height, may be rapid in its formation, and, provided it has not gone on to the stage of new tissue formation, may rapidly subside; and thus speaks strongly in favor of a mechanical, as opposed to a chemical or inflammatory, origin for the lesion.

Paralysis in the Left Recurrent Laryngeal Nerve in Mitral Affections.—Osler (*Arch. d. mal. d. cœur, d. vaisseaux et d. sang*, 1909, ii, 73) states that there are two valvular affections of the heart which may give the impression of an aortic aneurysm. The first, aortic insufficiency, as Corrigan pointed out, suggests it by the marked pulsation of the arch of the aorta. The second, lesions of the mitral valve, is even more confusing. To the paroxysms of cyanosis and dyspnœa may be added a visible pulsation in the second left interspace close to the sternum and a paralysis of the left vocal cord. Ortner (of Vienna) was the first to describe the compression of the left recurrent laryngeal nerve between the aorta and a considerably dilated left auricle, in a patient in whom he had diagnosticated aneurysm intra vitam. The majority of the cases have such a cause, but some few are due to compression by enlarged pulmonary veins or the left pulmonary artery.

Osler describes three cases within his experience, two of which were with autopsy. All three had signs of a double mitral lesion and paralysis of the left vocal cord. The second case gave a history of diphtheria, which, Osler emphasizes, may be the cause of the laryngeal paralysis in some cases. In this case, however, the change of voice antedated the attack of diphtheria. Autopsy in two of the cases showed the recurrent laryngeal nerve sclerotic and opaque in the portion compressed between the wall of the left auricle and the aorta.

A Simple Method for the Determination of the Diastolic Blood Pressure.—Ehret (*Münch. med. Woch.*, 1909, lvi, 606) alludes to the difficulty the general practitioner experiences in determining the diastolic blood pressure accurately. He describes a new method, which he has found accurate, simple, and easy of application. While the pressure is raised slowly in the cuff about the arm, one palpates the arteria cubitalis at the lower edge of the cuff. Without transition stages there will be felt,

very readily, a remarkable pulse wave, literally "springing up against the finger." The pulsation is so forcible that it is transmitted to the surrounding tissues. To the palpating finger the wave feels large, quick, and hard. In very fat, muscular arms, in which the arteria cubitalis is not readily felt, the phenomenon is somewhat more difficult to obtain. In such cases the finger is placed on the arm perpendicularly to the suspected direction of the artery. The pulse is perceived suddenly, and with it there is felt a pulsation communicated to the surrounding tissues. Many experiments have shown that the pressure at which this phenomenon occurs corresponds to that at which the greatest oscillation of the mercury column is seen.

Coagulation of the Blood in Thrombosis.—CHANTEMESSE (*Bull. méd.*, 1909, iii, 21) states that the coagulability of the blood is modified in the thromboses of cachexia, puerperium, hemorrhage, and infection. He increases the coagulating power of the blood by the calcium content determined by precipitation with increasing amounts of potassium oxalate. He believes calcium plays a rather active role in the coagulation process, and by following patients from day to day with this method he can prevent phlebitis or the formation of clots by administering such a decalcifier as citric acid.

Menstrual Hyperemia of the Liver.—CHVOSTEK (*Wien. klin. Woch.* 1909, xxii, 293) points out an intimate relationship between the female sexual organs and the liver. The frequent occurrence of icteris gravis and acute yellow atrophy during pregnancy, the appearance of attacks of gallstone colic during menstruation, the influence which must be attributed to pregnancy in the formation of gallstones, the frequency of fatty livers in women at the menopause and after castration—all these facts indicate a close relationship existing between the organs of reproduction and the liver in the female. In the literature the statement is made that there is a hyperemia of the liver during menstruation, but the statement is apparently not based on careful observations. Chvostek has percussed the liver borders in thirty women during and after the menstrual period and found that the lower border descended one to two finger-breadths in all but three. The swelling was noted in healthy and diseased livers with about equal frequency. There is no pain on palpation or percussion, and the enlargement is probably due to hyperemia.

An Unusual Localization of Lead Poisoning.—TELEKY (*Allg. Wiener med. Zeitung.*, January 5, 1909) confirms the theory of Edinger that the first localization of a toxin is in those muscles and organs which are being overworked. He describes as supporting evidence two cases of lead poisoning. Two sisters were employed in a factory rubbing the metallic wrappers of bottles. In this work the thenar eminence of the right hand was used particularly. And these two women presented themselves with atrophy and paralysis of the muscles of this eminence. They both gave a previous history of lead colic and encephalopathy.

SURGERY.

UNDER THE CHARGE OF

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Precocious Typhoid Cholecystitis.—Bobbio and Gennari (*Archiv. gén. de chir.*, 1908, ii, 555) reports a case in which, five days after the first signs of typhoid fever developed, the patient began to have the signs of a very acute cholecystitis. Operation two days later showed a necrotic gall-bladder, and two days after the operation the patient died. Typhoid bacilli were found in the bile. Up to the present time typhoid cholecystitis has been found to be rare and to develop especially toward the end of the fever or during convalescence. The greater number develop between the tenth and thirtieth days. The infection in Bobbio and Gennari's case was traced as follows: The bacillus of Eberth first invaded the blood and gave symptoms of acute septicemia. It became localized in the gall-bladder, where it gave rise to an increase phlegmonous inflammation. Migration of the bacilli then followed into the intestine, whither it was carried by the bile. The portal of entrance into the organism is doubtful, as is always the case. The diagnosis of the complication is sometimes far from easy, and an exploratory laparotomy is sometimes necessary. The statistics of Quenu show that of thirty operations done for cholecystitis during typhoid fever, seventeen were cholecystostomies and five cholecystectomies. While the latter is the ideal operation, it is in the majority of cases very grave.

Methodical Exploration of the Urethra.—Motz (*Ann. de mal, des org. gén.-urin.*, 1909, i, 161) says that the patient should not pass urine for some hours preceding the examination. The urethra is then expressed, and the secretion obtained is examined bacteriologically. The patient now urinates into three glasses, and the urine is examined by the naked eye and microscopically. The meatus first and then the glans and prepuce are cleansed with cotton moistened with oxycyanurate or bichloride of mercury (1 to 1000). The urethra is then irrigated with the oxycyanurate of mercury (1 to 3000), containing a few drops of methylene blue, and the bladder filled. The region as far as the bulb and Cowper's glands is expressed and the patient asked to urinate 15 to 20 c.c. of the bladder fluid. This is examined for filaments or a cloudy fluid, and it is preserved for a microscopic examination. The patient then lies recumbent again and a methodical examination is made of the prostate, seminal vesicles, and membranous urethra. Their contents are expressed into the urethra, and the patient again urinates about 100 grams of the bladder fluid, this being divided into two glasses if it is cloudy. To the first should be added a few drops of

acetic acid, to see if the cloudiness disappears. If it persists, the second glass is kept for microscopic examination. The caliber of the urethra is then examined, beginning with a No. 25 exploring instrument. A larger bougie, No. 46, is then introduced into the urethra and the wall of the anterior urethra examined for any infiltration in it. If it seems to show an impalpable gonorrhœal focus, the urethra is massaged and the patient asked to urinate. The fluid obtained is retained and examined for trouble in the glands of the anterior urethra. All these explorations can be made at one sitting. Two or three days later a urethroscopic examination should be made. It is preceded by an irrigation of the whole urethra and filling of the bladder. When on account of a stricture or rebellious spasm of the urethra all the antiseptic precautions referred to above cannot be carried out, it should be borne in mind that every attempt at catheterization may prove septic, because of microörganisms in the normal urethra. After the examination is completed in such a case a small enough catheter should be passed into the bladder and a weak solution of silver nitrate (1 to 200) injected into the bladder and along the urethra. In this way the complications resulting from exploration are reduced to a minimum.

The Treatment of Severe Strictures of the Œsophagus by Œsophagostomy.—Guisez (*Archiv. gén. de chir.*, 1908, 562) says that of 28 cases of cicatricial strictures of the œsophagus, in 23 the normal caliber was reached and the patient returned to normal or nearly normal alimentation. In those cases in which failure resulted the strictures were entirely closed or a filiform could not be passed. The results were in all cases better the more recent the strictures. The short valvular strictures seem to be especially benefitted by this method. Multiple strictures offer no serious obstacles to endoscopy, each stricture being dilated successively. Long strictures with longitudinal infiltration alone are difficult to dilate and to keep dilated. The results, taken as a whole, are very satisfactory, since in four-fifths of the cases a cure was obtained, although in some a gastrostomy would have been the only palliative operation which would have prevented the patient from starving. Gastrostomy is itself not without danger, and in children it is rare that it gives long service.

Extravesical Suprapubic Prostatectomy.—Stockum (*Zentralbl. f. Chir.*, 1909, xxxvi, 41) says that the perineal operation is undoubtedly less dangerous than the suprapubic, but that it has the disadvantage of leaving behind, occasionally, rectal and urethral fistulæ. Stockum did the following operation in two cases with good results. The patient was anesthetized and placed in a marked Trendelenburg position. A soft catheter was placed in the empty bladder and a median suprapubic incision made. The prostate and beginning of the urethra were rendered visible by passing between the symphysis and bladder, and hooking the anterior peritoneal fold upward with the finger. A small opening was made in the highest portion of the capsule of the prostate, which could be enucleated through this opening without working through the bladder, the catheter in the urethra helping to locate the latter. During this stage the prostate was pushed upward by the finger of an assistant in the rectum. There was considerable bleeding, but a gauze

tampon inserted controlled it. To drain the urine from the bladder a small buttonhole was made in the summit of the bladder and a rather thick drainage tube introduced and fixed to the bladder wall by a catgut suture. The abdominal wound was clased down to the tube and gauze drainage introduced. The urine was conducted to a glass bottle at the side of the bed containing a 1 to 1000 bichloride solution. The hemorrhage was free for a few hours, but stopped spontaneously. The urine flowed freely and was slightly blood stained. The large gauze drains were removed on the second day and were replaced by strips of gauze. The bladder was washed out daily with a weak silver nitrate solution through the drainage tube. On the fifth day the gauze and rubber drains were removed and a silk catheter introduced through the urethra. This was removed on the twelfth day, when the bladder and urethral wounds were closed and the patient urinated spontaneously. Stockum considers that this operation is more simple than the Freyer and makes a smaller wound. Blood is not so likely to get into the bladder as in a Freyer operation, and, therefore, the catheter is not so likely to become obstructed by blood clot.

Apparently Strangulated Herniæ.—CLAIRMONT (*Archiv f. klin. Chir.*, 1909, lxxxvi, 631) says that an apparent strangulation of an external hernia may result from a mechanical or paralytic ileus. An inguinal, femoral, or umbilical hernia, free until that time, may become irreducible and somewhat painful and tense. The simultaneous existence of signs of intestinal obstruction may lead to the diagnosis of an incarceration of the external hernia. The changes in the hernia, however, depend upon and are secondary to the intra-abdominal trouble. Damage may be done to the hernial contents, now irreducible, in view of the crowded condition of the sac and the increasing distention of the intestine within. The causal relations may be reversed, that is, a primary incarceration may be followed by a second intra-abdominal occlusion of the bowel. The most important evidence showing a strangulation is to be found in the slight degree of tension and pain in the hernia. The condition which underlies the false strangulation or is merely associated with a real strangulation, may be determined to be a mechanical or a paralytic ileus, but only in rare cases can it be exactly diagnosticated. If a supposed strangulated hernia be wrongly diagnosticated and be operated on, the herniotomy will occasionally indicate, by the atypical findings, an intra-abdominal complication. If the symptoms of ileus persist after the operation or reduction of a supposed incarcerated hernia longer than twenty-four hours, one should think of an unrelieved mechanical or paralytic ileus. The prognosis of these cases is unfavorable. Improvements can result only from a proper interpretation of the clinical picture, early surgical intervention, and exact attention to the anatomical findings. The best treatment is a hernio-laparotomy.

The Extirpation of Brain Tumors in the Motor Cortical Area.—MIYAKE (*Archiv f. klin. Chir.*, 1909, lxxxviii, 811) says that there are three principal views as to the operative treatment of brain syphilis. The supporters of the first say that operative treatment should be rejected and antisyphilitic treatment exclusively recommended. This is the view

of most neurologists and internists. According to the second, operative treatment is indicated only under certain circumstances, chiefly after the failure of antisyphilitic therapy. Most surgeons and a few internists entertain this view. According to the third view, all antisyphilitic treatment should be rejected and only operative carried out. An analysis of the cases of brain syphilis operated on shows that the diagnosis has not always been correctly made or the exact situation of the tumor established, but the operations were done upon the doubtful diagnosis of brain tumor and a syphiloma accidentally found, as in Miyake's case. He thinks that when the internal treatment fails, and the syphilitic tumor is favorably situated, it should be operated on, as the permanent results will be better. In his patient antisyphilitic treatment continued for fifty days was entirely without results. Extirpation was followed by strikingly prompt success. The patient not only recovered quickly, but showed only insignificant functional disturbances in the affected limb, and these later disappeared.

Experimental Investigations Concerning the Preventive Influence of Hirudin upon Coagulation of the Blood in Animals.—RIMANN and WOLF (*Deut. Zeit. f. Chir.*, 1909, xcvii, 177) carried out their experiments to determine whether by the introduction of drugs into the circulation, the development of thrombosis could be hindered. They employed for this purpose hirudin, the value of which in preventing coagulation was first demonstrated by Haycroft in 1884, and which has been more recently studied by Peckelharing and others. Rimann and Wolf concluded from their studies that in order to delay the coagulation of circulating blood for a certain time, in small dogs, it was sufficient to inject intravenously a quantity of hirudin, which would give 0.005 gram for every 50 c.c. of blood. The time during which the preventive action on coagulation of this dose (half the normal dose) lasted was between one and one-half and three and three-quarter hours. With an intravenous injection of 0.019 of hirudin for every 50 c.c. of blood (normal dose), coagulation occurred first after four and one-half hours. Subcutaneous injection of hirudin exerted no influence upon the coagulability of the blood. Injurious influence of the hirudin in the established dose upon the general condition could not be determined.

Congenital Dislocation of the Lower End of the Ulna.—ROBINSON and JACOULET (*Archiv. gén. de chir.*, 1909, iii, 1) says that with regard to the pathogenesis of congenital luxation of the lower end of the ulna we ought to take into consideration two factors, the anatomical and mechanical. The anatomy shows us that the radial incurvation and posterior luxation of the lower end of the ulna are only an exaggeration of a congenital disposition of the bones and inferior radio-ulnar articulation. The congenital tendency existing, the deformity is accentuated by the muscular contractions applied in the occupation of the patient. According to this theory the intervening cartilage undergoes modifications purely mechanical. It is possible that sometimes there may be an infectious lesion of the cartilage, but up to the present time this has not been demonstrated. The kyphosis of the carpus presents some analogies with genu valgum on the one hand, and congenital dislocation of the hip on the other. There are only a few chances that surgical intervention will prove really efficacious.

THERAPEUTICS.

UNDER THE CHARGE OF

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The Action of Intravenous Injections of Strophanthin in Heart Disease.—DANIEL POLU (*Archiv. d. mal. d. cœur.*, 1908, xi, 609) has given intravenous injections of strophanthin in 23 cases of heart disease with very encouraging results. He believes that strophanthin is one of the best heart stimulants, not only because of the rapidity with which it acts, but also because of the possibility for securing accurate dosage and because its action is exerted exclusively upon the heart. He used 0.001 gram ($\frac{1}{64}$ grain) of the strophanthin, repeating the dose at intervals of twenty-four hours, for several days if necessary. As a rule, one or two injections were all that was necessary. It acts more rapidly than any other known heart stimulant, he says, increasing the force of the contractions, slowing the pulse, raising the arterial tension, and increasing the amount of the urine notably. Consequently the œdema and the passive congestion of the viscera soon subsided. These effects were especially marked when there was no advanced kidney lesion. When the kidneys are markedly deficient, strophanthin is useless unless combined with diuretics. In a few cases good results were obtained by the combined administration of theobromin by mouth and strophanthin intravenously. For this reason he believes, with Lust and Hoepffner, that the injection of strophanthin may serve to differentiate whether the trouble is a primary cardiac failure or heart failure secondary to an advanced nephritis. He had no complications, such as fever or chills, after the intravenous use of strophanthin, and believes that they can be avoided by strict asepsis.

The Treatment of Degeneration of the Myocardium with Intravenous Injections of Strophanthin.—FLESCH (*Wien. klin. Woch.*, 1908, xlvi, 1590) reports only a single case, but the benefit was so striking after the failure of all other heart stimulants and diuretics that he cannot refrain from attributing some credit to the strophanthin. He used 0.001 gram intravenously at intervals of two or three days. He was able by this treatment to keep his patient in good condition for months.

Atropine in the Treatment of Bronchial Asthma.—TERRAY (*Med. Klinik.*, 1909, iii, 79) speaks for the wider use of atropine in the treatment of bronchial asthma. He believes it exceedingly valuable for certain cases, especially those with a marked neurotic element. Terray cites the histories of seven severe cases of bronchial asthma treated by atropine with very encouraging results. In one of these cases he not only succeeded in arresting the acute attacks, but the patient was so much improved that there was no recurrence of attacks for ten months.

Previously, this patient had been constantly affected for twenty years. He prescribes atropine in pills, each pill containing 0.0005 gram ($\frac{1}{120}$ grain). He gives one pill a day at first, then, after two or three days, gradually increases the dose to a total of from four to six pills a day. When this amount has been reached, he gradually reduces the amount to one pill a day. Terray believes that atropine not only will arrest an attack, but it also will prevent a recurrence. One great advantage is that atropine can be advantageously used as a substitute for morphine or may be alternated with morphine.

The Limitations of the Treatment of Neuralgia by Injection.—SCHLESINGER (*Med. Klinik.*, 1908, xlix, 1868) has been using physiological salt solution just below the freezing point for the local treatment of neuralgia. The advantages of the chilled solution are the small volume of the injection and the immediate relief to the pain, which is most encouraging to the patient. He cites sciatica as a type of painful nerve affection in which many observers have reported beneficial effects from the injection therapy. He believes that many cases of sciatica which have been reported as cured or benefitted by the injection treatment are of questionable diagnosis. He insists that an accurate diagnosis is essential, and believes that all cases of acute sciatica and the majority of the chronic cases do not improve under the injection treatment. Such cases should be treated by rest in bed, quinine in small doses, and galvanization. The latter should not be begun too early. Schlesinger gives the distinguishing features of true sciatica, and also calls attention to the fact that sciatica may be a gouty manifestation and yield to appropriate treatment for gout.

Furthermore, he believes that intraneural injections are dangerous for mixed nerves like the sciatic. He has seen paralysis result from such an injection. Schlesinger describes an affection which he considers different in many ways from true sciatica and which is very amenable to injection therapy. This begins gradually with a little sensitiveness in the hip, vague drawing sensations which only gradually develop into intense pain, whereas sciatica, as a rule, develops suddenly. Furthermore, this non-sciatic pain does not follow the course of the sciatic nerve, but spreads over the surface from the crest of the ileum to the spine. This pain area may be as large as the palm of the hand, and the overlying skin is always hyperesthetic to a greater or less degree. This group of symptoms differs considerably from sciatica, in which complaint the skin is usually less sensitive than normal. Furthermore, these areas are not innervated by the sciatic nerve. He believes that this trouble is due to a neuritis of the smaller nerve fibers in the muscles, and that the pain is produced by traction upon the periosteum by the contraction of the muscle bundles. The localization of the most painful area at the crest of the ileum at the insertion of the muscle can be thus explained. This affection can be cured by the injection of any of the different solutions advised for the purpose, such as the injection of 50 to 100 c.c. of an 8 per cent. salt solution with a little cocaine, the Lange technique; the injection of the same solution at different points, the Peritz technique; the injection of 10 c.c. of Schleich's solution, Alexander's method; or by the injection of 10 c.c. of salt solution just below freezing point, which is Schlesinger's method. Schlesinger

condemns the use of alcohol injections as too dangerous. He says that even with the best technique the nerve is often missed. The sharp lightning pain is not an absolute indication of the entrance of the needle into the nerve, since the needle may strike the periosteum and give rise to similar pain. The abundant work done with nerve injections, Schlesinger says, has brought out two main facts. The first is that the beneficial effects of the injections are often very uncertain. The second is the deficient knowledge of the anatomical causes of neuralgic pain.

Use of Alkalies in Practical Medicine.—SMITH (*Brit. Med. Jour.*, 1909, i, 263) enumerates the various uses of the alkalies, especially their action in modifying the digestive functions. He believes that they must be used with discretion, for appropriate conditions, and on a definite plan. They should be used only in moderate doses, and should be immediately discontinued when their administration shows no definite beneficial effects. The alkalies have a local action on the stomach and intestinal tract, which, Smith believes, is due more to their influence in restoring the deranged functions of the gastric mucosa in catarrhal conditions than to their chemical action upon the gastric secretion. Besides this local action, Smith ascribes to the alkalies a more general effect upon the body metabolism.

In gastric disturbances, sodium and potassium bicarbonate seem to be equally good. Smith believes that the action of the alkalies is enhanced by the addition of a few grains of sodium chloride to each dose. If the stomach is very irritable, the alkalies should be made to effervesce with citric acid. The caustic alkalies—liquor potassæ and liquor sodæ—have a more marked sedative action upon the stomach than the bicarbonates. The heavy carbonates of magnesium or calcium carbonate are often useful. Smith advises the use of the insoluble alkalies for the purpose of neutralizing acid formed in the cecum. He thinks these are likely to pass unaltered through the stomach and reach the lower bowel unchanged. Smith also discusses the use of alkalies in the treatment of urinary acidity, in urinary sand or gravel, and in suppression of urine. He speaks of the beneficial effects in viscid bronchitis and of the value of sodium citrate in infant feeding.

Antibacterial or Antitoxic Immunization in Tuberculin Treatment.—TRUDEAU (*Jour. Amer. Med. Assoc.*, 1909, iv, 261) discusses the two widely differing theories of the mode of action of tuberculin therapy. One of these is the "vaccination" theory, which claims, as a result of the tuberculin treatment, a greater or less degree of a specific immunity to the tubercle bacillus itself. The "toxin immunization" theory holds that there results an immunity to the toxin of the tubercle bacillus. Trudeau believes that until more accurate knowledge is obtained of the mode of action of tuberculin, opinions will differ as to the best method to be employed. He also believes that neither theory is entirely satisfactory. He says that the production of a general antibacterial immunity in not supported by experimental evidence. On the other hand, in cases of purely localized tuberculous disease, in which the general health is unimpaired and there is no evidence of chronic toxemia, the use of tuberculin is often attended with good results. It is evident that this

result is not caused by an antitoxic action, though it may be due to many imperceptible focal reactions and not to a general specific immunity. For a working theory Trudeau prefers the conception of the production of an immunity that is principally antitoxic.

Trudeau concludes as follows: If we accept the toxin immunization conception as the essential feature and guide to the treatment, instead of measuring the degree of a questionable antibacterial immunity by the opsonic index, or attempting to produce it more or less empirically by a series of moderate reactions, the severity of which we cannot in any way control, the main features in our treatment would be: (1) To raise the degree of tolerance to tuberculin to the highest point attainable in each case by an almost imperceptible and long-continued progression in dosage. (2) To avoid general and focal reactions as much as possible and consider them merely as evidences of intolerance. (3) To follow no arbitrary rule as to rate of increase or the maximum dose to be reached, but to be guided merely by the degree of toxin tolerance of each patient as shown by the symptoms and general condition, whether the highest individual maximum dose attainable be only a small fraction of a milligram or a cubic centimeter or more.

The Treatment of Bronchial Affections by Raising the Foot of the Bed.—SCHÄFER (*Deutsch. Archiv, f. klin. Med.*, 1909, iii, iv, 376) gives a report of 29 cases of various forms of bronchial affection treated by raising the foot of the bed, as advocated by Quincke. The patients first lie flat in bed on the back with the head turned to one side. When they have become accustomed to this position, the foot of the bed is raised from eight to twelve inches for two or three hours every morning. In some of the cases, this procedure was also made use of in the evening. The patients were enabled to raise large amounts of sputum by this method, and during the remainder of the day had little or no cough and no expectoration. The fever resulting from the retained secretions rapidly subsided and the patients increased in weight. This method is especially valuable, Schäfer says, for all cases of bronchiectasis of the lower lobes and for the long-protracted cases of bronchitis in elderly people.

Combined Intravenous Arsenic and Tuberculin Therapy.—Wendell (*Münch. med. Woch.*, 1909, lii, 13) speaks of the good results obtained by the combined treatment with atoxyl and tuberculin. He advises Koch's old tuberculin in doses of $\frac{1}{100}$ to $\frac{1}{10}$ mgm. injected intravenously every eighth day. Atoxyl in gradually increasing doses from 0.05 gram to 0.3 gram is injected every second day. Wendel believes that the tuberculin causes a hyperemia about the areas of tuberculous infiltration, and that consequently atoxyl is brought in larger amounts to these areas. Therefore the atoxyl exerts its healing action at the site of the tuberculous process. In addition, the tuberculin aids by the production of antibodies. In the cases Wendel treated by this method he noticed both an improvement in the local process and in the general condition of the patient. He says that this plan of treatment is suitable not only for hospital cases, but also for ambulant cases without fever in the first or second stages of the disease.

The Treatment of Internal Hemorrhage by Sodium Chloride.—Von den Velden (*Deutsch. med. Woch.*, 1909, v, 197) relates some interesting experiments upon animals and normal individuals, which seem to show that sodium chloride has a distinct influence in increasing the coagulability of the blood. He found that, after doses of from 5 to 15 grains of sodium chloride by mouth, there was an increase in the coagulability of the blood, reaching its maximum in from seven to fifteen minutes and persisting for from one to one and a half hours. He remarks that sodium chloride does not have this action in test-tube experiments, and attributes the increase in coagulability to a mobilization of the thrombokinase stored up in the tissues. Sodium chloride has long been a popular remedy for hemorrhage, and its beneficial effects have been ascribed to a hyperemia of the splanchnic area due to nausea. The author points out that in the doses he used, this nauseating action could largely be excluded; in fact, he tried to avoid any nauseating action. His clinical results support the experimental evidence. In 29 cases of hemoptysis he obtained excellent results by the administration of 5 grams of sodium chloride by mouth. It is interesting also to note that he obtained similar results by the use of bromides. With a recurrence of the hemorrhage, he repeats the sodium chloride or substitutes sodium or potassium bromide. In addition the bromides have a general sedative action. He keeps up the combined sodium chloride and bromide treatment in severe cases, giving from 20 to 30 grams of sodium chloride and from 12 to 15 grams of bromide during the day. The sodium chloride corrects any tendency to bromide poisoning. When it is essential not to irritate the gastro-intestinal tract, as in hemorrhage from the stomach or from typhoid ulcers, he prefers to give the sodium chloride by infusion. For this purpose he uses from 3 to 5 c.c. of a sterilized 10 per cent. solution. The intravenous method is also to be prefered, he says, to prolonged and large dosage by sodium chloride when there is a suspicion of an inefficiency of the kidneys. The author believes that this treatment is of no value in such hemorrhagic diseases as hemophilia which are not influenced by transitory increases in the coagulability of the blood.

A New Digitalis Preparation.—Müller (*Münch. med. Woch.*, 1908, li, 2651) writes of the results obtained at the Heidelberg clinic by the use of digipuratum (Knoll). Digipuratum is an extract of the active principle of digitalis leaves. It may be obtained in tablet form, each tablet containing 0.1 gram, or in powder form. It is insoluble in cold water and acids, but easily soluble in dilute alkaline solutions. Müller advises its use in all cases of cardiac insufficiency, whether of valvular, vascular, or muscular origin. Its action is similar to that of other digitalis preparations, but it is lacking in most of the unpleasant secondary effects. The good effects are obtained generally after 1.2 grams given in doses of 0.3 to 0.4 gram per day. Sometimes its effects are not noticed until 2 to 2.5 grams have been given. Digipuratum is especially well borne by the stomach, and has none of the unpleasant gastro-intestinal symptoms of other perparations. When the remedy is to be used over a long period of time, 0.05 gram per day will be sufficient to continue the therapeutic effect of the drug.

PEDIATRICS.

UNDER THE CHARGE OF
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Tuberculin Reaction, with Special Reference to the Auricular Reaction.—V. TEDESCHI (*Archiv f. Kinderheilk.*, 1909, xlix, 190), writing under this title, states that the activity of the tuberculin is of more importance in the production of the specific tuberculin reaction than is usually believed; it is well known that the tuberculins are not identical, that they are not prepared in the same manner, that they do not produce reactions over the same periods of time, and that they are not equally active in the same degree of solubility. Of further importance in the tuberculin reaction are the age of the patient, the different types of tuberculosis, and the various intercurrent diseases, since even some of the tuberculous changes themselves have an influence on the intensity and appearance of the reaction. Another point of importance is whether the tuberculin is of animal or human origin. Using both simultaneously on the same patient, it has frequently occurred that one produces a positive, the other a negative reaction. Tedeschi, therefore, advises the employment of both types of tuberculin simultaneously, and considers it of paramount importance to improve the technique of the reaction. Calmette's procedure he considers too dangerous and too uncertain on account of the hyperemic state of most eyelids in lymphatic children. He prefers v. Pirquet's method, modifying it to some extent. He injects very minute, carefully measured quantities of tuberculin beneath the skin. While this improves the certainty of the results considerably, the looseness of the subcutaneous tissues makes the recognition of indurations difficult, especially if they are but slight. Various parts of the body were tried, the auricular tissues giving the best results, because of the density of the underlying structures and their vascularity. Tedeschi sums up his results as follows: The auricular reaction is as devoid of danger as the dermal reaction; it possesses fewer sources of error than the other methods, particularly the ocular reaction. It is preferable to the ordinary dermal reaction as the consequences of either too deep or too superficial incisions are prevented. The deeper infiltration is more easily made out than in other methods on account of the transparency of the structures, and is more evident to the touch on account of the cartilaginous base. The reaction is more accurate; it permits the measurement and judgment of the employed fluid, particularly in reference to the comparative quantities of tuberculin, and the weight and age of the patient.

Sulphur Water Cures in Children.—O. HEUBNER (*Therap. Monats.*, 1908, xxii, 605) sees no reason why children should not be permitted to drink mineral waters as well as adults, and particularly recommends sulphur water in the form of drink, gargle, or inhalation for the chronic

pharyngeal catarrhs of children. Such catarrhs, whether caused by adenoids, enlarged tonsils, or other conditions, are associated with loss of appetite, constipation, anemia, frequent vomiting, etc. The latter occurs in most instances during the process of eating. The teeth are usually carious, and the throat and back part of the tongue are covered with foul-smelling exudate, which does not yield to any of the treatments usually ordered for it. He advises sulphur water for these catarrhs, and says he has had excellent results. He orders a wineglassful at waking, a second one a half-hour later, and another during the evening hours; it is used cool, as its taste is then less objectionable. Adenoid growths must be removed to get the best results. The use of sulphur water has never been followed by bad consequences.

Experiments with Albulactin in Artificially Fed Children.—Albulactin is the albumin of cow's milk; it is of a pure white color and is readily soluble in water. If hydrochloric acid is added to ordinary diluted milk, a coarsely granular precipitate forms, which makes a firm deposit within a short time; if the acid is added to a 1 per cent. solution of albulactin, a finely granular precipitate is produced, just as in mother's milk; it remains so throughout digestion. J. CASSELL and H. KAMMITZER (*Archiv f. Kinderheilk.*, 1909, xlix, 168) added albulactin to the food of a number of children, most of whom were in good health, but somewhat poorly nourished; a few of the children were suffering from different diseases. The albulactin was dissolved in their food, and no difficulty was observed in feeding the children. In a number of instances the food was again withdrawn after a varying period of time and tested for reaction, free and combined acids. The results were equally good in the normal and the sick children. The general state of health always improved, even in the badly nourished infants; there was never any vomiting or diarrhœa, nor did the urine ever contain albumin. The motor function of the stomach remained good with albulactin in all cases but one, in which dyspepsia resulted, due to a concentrated state of the cow's milk given the baby. The amount of free hydrochloric acid was normal in 5 of the 7 instances in which it was tested. The stomach contents removed in cases in which albulactin was added consisted of fine granules; the infant's stomach is more tolerant of these, and they distribute themselves better than the tough, coarse masses present when albulactin was not used. The weight of the children improved splendidly and the albulactin children had a better and rosier appearance than the others, their flesh becoming much firmer under its use.

Scarlet Fever Carriers.—C. HERRMAN (*Archives of Pediatrics*, 1909, xxvi, 112) believes that desquamation is an unimportant factor in the spread of scarlet fever. He has often seen desquamating children play with other children, who did not contract the disease. Infected rooms are much more commonly at the bottom of furthering the disease. Another factor is the throat of an individual not really ill with the disease, but acting as host to the microörganisms. The most important cause, however, lies with the patients themselves, who may retain the causal agent for a long time (even months) in the secretions and discharges of the nose, mouth, ear, etc. From 30 to 50 per cent. of con-

valescing scarlet fever patients have discharging noses and ears. Mild scarlet fever cases are often not diagnosticated, but may still act as scarlet fever carriers through the discharges mentioned. Isolation should be strictly enforced during an epidemic, and the children of a family having a scarlet fever patient should not be permitted to attend school. Nasal and oral hygiene should be enforced; adenoids, tonsils, and carious teeth removed or treated. Disinfection of the premises after scarlet fever should never be neglected.

The Therapeutic Use of Tuberculin in the Tuberculosis of Children.—A. SCHLOSSMANN (*Deut. med. Woch.*, 1909, xxxv, 289) has employed tuberculin in the treatment of a small number of tuberculous children. He states that tuberculin is a specific agent in the tuberculosis of children; it favors complete cures. Only when large doses are employed will the organism of the tuberculous child react to the drug by formation of antibodies. In beginning treatment with tuberculin he first endeavors to make the organism tolerant against the drug (period of small doses); during the longer period of treatment with larger doses in appropriate intervals the formation of antibodies should be assisted and made permanent. Ill results due to the tuberculin during the period of treatment with large doses were not observed.

Scarlet Fever following a Wound in the Foot.—F. VAN DER BOGERT (*Archives of Pediatrics*, 1909, xxvi, 126) reports the case of a boy, aged five years, who stepped on a "rusty" nail. After two weeks the wound had healed and the boy was again running around barefoot. On the sixteenth day the site of the injury was again inflamed; the inguinal glands of the corresponding side were inflamed, large, and painful. Within two days he developed a typical scarlet fever rash, a strawberry tongue, a typical angina, cultures from which showed no diphtheria organisms. The opposite inguinal glands were also enlarged by this time and the boy's temperature reached 104°. Albuminuria developed and epistaxis was noted several times. The wound in the foot broke down and pus from it contained a pure culture of streptococci, as did also the throat. The desquamation was typical. A younger sister also developed scarlet fever. The author believes that the scarlet fever virus entered the wound between the fourteenth and sixteenth day after the injury, during the time when the boy again walked barefoot. The incubation period was probably two to four days.

OBSTETRICS.

UNDER THE CHARGE OF

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The Surgical Treatment of the Umbilical Cord.—BALLANTYNE (*Brit. Med. Jour.*, April 17, 1909) draws attention to the risks of infection at the umbilicus in cases treated by the ordinary method of ligating

the umbilical cord. He quotes Keller's statistics, giving a mortality of 2 per cent. in children, due to umbilical infection during the first month of life. Ballantyne has found that in premature children the umbilical vessels close less promptly than in children at full term, and hence the risk of infection is greater. To overcome this, and to treat the cord by surgical methods, Ballantyne tried seven different plans of dealing with the cord. In the first method the cord was cut with scissors one and one-half inches from the umbilical ring, the fœtal end grasped between the thumb and forefinger, the vessels ligated separately with No. 1 catgut, and the sheath of the cord stitched over the resulting stump with fine silk sutures. In cases so treated a dry, black scab formed at the umbilicus, the child recovered without jaundice, and apparently did well.

By the second method the clamp was applied to the cord one inch from the umbilicus, the stump was crushed, and the clamp removed without bleeding. The sheath was sewed over the stump with a continuous silk suture. No ligature was applied, as the pressure of the forceps had stopped the bleeding. This method gave good results, and seemed, if anything, better than the first method.

In the third experiment the sheath of the cord was cut through with a scalpel in a circular fashion, one and one-half inches from the umbilicus. The silk ligature was tied around the whole cord, and the cord cut short. The edges of the sheath were brought together with silk sutures. This method resulted well.

In the fourth method an effort was made to cut the sheath of the cord on the fœtal side and secure the vessels, and then pull the reflected sheath over the vessels and stitch it in place. This was found difficult because of Wharton's jelly.

In the fifth method the cord was cut in a circular fashion, the vessels picked up separately with artery forceps and ligated with catgut. Some difficulty was found in the ligature slipping; the sheath was stitched over the stump, and, on the whole, the method resulted well.

In the sixth method the sheath of the cord was cut in a circular fashion near the umbilicus, the cord transfixed with a needle and ligature, the two halves being separately tied. The cord was then cut outside of the ligature and the sheath stitched over. A small black scab formed at the umbilicus, but the result was good.

In the seventh method the cord was cut off flush with the skin of the umbilicus, and the skin surfaces were joined. A circular incision was made at the junction of the skin with the sheath of the cord. The vessels were separated from the jelly and tied separately. The cord was severed, and the edges of the skin were then united with catgut.

The operation required ten minutes. The stumps healed like ordinary surgical wounds in aseptic condition, no putrefactive changes occurred, the surfaces uniting by first intention. There seemed to be less than the usual risk of slipping of the ligatures, and hemorrhage. The only objections to this method were the time taken in doing the operation carefully and the fact that the medical attendant will be called upon to do this operation at a time when the mother's condition might demand his attention. There seems to be no good and sufficient reason why the umbilical stump should not be ligated and closed like any other surgical wound, and if this be done properly putrefactive changes need not occur, and union should result by first intention.

The Prevention of Puerperal Fever.—An editorial writer in the *British Medical Journal*, April 24, 1909, draws attention to the fact that no positive decision has yet been reached as to what may safely be done in the prevention of puerperal fever. Hofmeier's report of 10,000 cases at Würzburg shows 15.36 per cent. of abnormal cases; in 11.48 per cent. the temperature rose above 100.4°. Among the 10,000 women 9 died with puerperal infection, the mortality of the clinic being 0.04 per cent. Among these patients, vaginal examinations were made, but a thorough disinfection of the hands was practised by students and midwives, and the external genitals of the patients were also treated in an antiseptic manner. Henkel relies on hot water and alcohol to disinfect the hands, and the use of rubber gloves. Scanzoni, in 157 precipitate births, had 97 cases who had no vaginal examination before the expulsion of the child; 21.6 per cent. of these patients had fever. In 112 women delivered without contact from without 11.5 per cent. had fever. These cases indicate that the genital tract may contain sources of infection independent of the bacteria conveyed by examination.

Fibromyoma of the Pregnant Uterus Producing Occlusion of the Intestinal Tract.—Bachmetew (*Zentralbl. f. Gynäk.*, No. 16, 1909) reports the case of a pregnant woman who had in the abdomen, evidently upon the uterus, a small tumor. When four or five months pregnant she suffered with severe pain in the left lower portion of the abdomen, extending down the left lower extremity. These pains were so severe that she entered the hospital. On examination a fibroid tumor complicating pregnancy was diagnosticated. The patient suffered from obstinate constipation which could not be relieved. Vomiting and tympany developed, and upon examination under ether, stenosis of the bowel could be clearly made out. The uterus was emptied by dilatation with an elastic bag, followed by version and extraction. This, however, produced no relief and the abdomen was opened. The transverse colon was found adherent to the uterine fibroid, which was covered by omentum and mesentery, also adherent. In separating the adhesions the covering of the bowel was torn, and repaired by sutures. The tumor was removed and its pedicle ligated, and two small, subserous fibroids of the uterus were also removed. The appendix was found distended with fecal calculi and inflamed, and was removed. The patient made a good recovery. On examining the tumor it was found to be a fibromyoma of the uterus undergoing necrosis.

Complete Extraperitoneal Cesarean Section.—Freund (*Zentralbl. f. Gynäk.*, No. 16, 1909) reports the case of a primipara having a flat rachitic pelvis with a true conjugate of 7 cm. A long transverse incision was made and the lower uterine segment exposed in the usual manner. The bladder was readily pushed out of the way, and the uterus opened in the median line. A full term child was readily delivered by forceps, and the placenta removed by Créde's method. The incisions were easily closed by sutures, the patient making an uninterrupted recovery, without drainage. He also reports a second case of a multipara with flat rachitic pelvis, upon whom the same operation was performed. An assistant was enabled so to manipulate the uterus as to bring it in the

most favorable position for incision, and also to assist by pressure in bringing the child into the uterine wound. There was some tendency to uterine relaxation, which yielded to injections of ergot. This patient also made a good recovery. In these operations no attempt was made to push the bladder out of the way by distending it with sterile fluid. The manipulation of the uterus, bringing it to a favorable position for section, was very useful, and rendered unnecessary the employment of instruments for holding the bladder out of the way and holding asunder the edges of the incision. The manipulation of the child's head to bring it into the incision was also useful.

The Toxemic Vomiting of Pregnancy.—HENDRY (*Jour. Obst. Gyn. Brit. Empire*, April, 1909) reports the case of a primigravida, aged nineteen years, admitted to the Liverpool Maternity Hospital with grave emaciation, moderate jaundice, a temperature of 97° F., a weak and thready pulse, 90 to 100, feeble heart sounds, a furred tongue, and oral and dental sordes. Vomiting was frequent without food. The child was living. The patient was in the twenty-eighth week of pregnancy. The urine was scanty; specific gravity 1020; acid; bile stained; containing albumin and mucus, but no casts. The patient was fed with milk and water, and the urine examined, finding urea 1.27 per cent.; ammonia with a percentage of urea of 14.7. Labor gradually developed; the amniotic liquid had a specific gravity of 1010, alkaline; was dark gold and yellow in color, and gave a reaction for bile upon examination. A seven months' fœtus, not jaundiced, was spontaneously expelled. The patient made a gradual recovery, the percentage of urea rising and the percentage of ammonia decreasing. The ammonia varied in this case from 14.7 per cent., just before delivery, to 4.6 per cent. eight weeks after delivery. Leucin and tyrosin were absent. Acute yellow atrophy of the liver was excluded by the gradual onset of the condition, the slight jaundice, the absence of cerebral symptoms, the normal liver dulness, and the recovery of the patient. The infant lived but a few hours after delivery.

Bacterial Vaccines in the Treatment of Septic Infection.—OASTLER (*Amer. Jour. Obst.*, April, 1909) reports in detail a case of chronic sepsis steadily growing worse, treated by bacterial vaccines. In this case both Fallopian tubes were removed by median abdominal incision. This condition followed puerperal septic infection. The patient recovered after treatment continued for three and a half months. A second case of acute gangrenous appendicitis with thrombosis, pyemia, and abscess of the liver, recovered after several months' treatment. The third case of septic endometritis from criminal abortion also recovered. The conclusions reached by these cases are that apparently favorable results have been obtained by the vaccines of streptococcus, staphylococcus, Bacillus coli communis, Bacillus mucosus, and gonococcus. All but the gonococcus vaccines should be autogenous. The vaccines aid in combating the septic processes and are especially required when the blood shows a low leukocyte count with high polymorphonuclears. In violent cases of acute sepsis no resistance can be created and no effect is obtained. The positive phase is more often obtained than the negative. Blood cultures are generally negative. The wound

discharge increases soon after injection. The pulse remains rapid some time after the temperature falls, but as yet there have been no ill effects from the injection. The dosage is purely experimental. Too large a dose does harm, and small doses give better results than large. The site of injection and the frequency of injection can only be determined by trial. The following doses every fourth day were found beneficial: Staphylococcus, 160,000,000 to 325,000,000; streptococcus, 40,000,000 to 80,000,000; Bacillus coli communis, 40,000,000 to 150,000,000; Bacillus mucosus up to 110,000,000; gonococcus 6,000,000 to 80,000,000. If the negative phase appears, the injection should be delayed and the dosage reduced. The opsonic index is an uncertain indication. The best indication of the resisting power of the patient is the leukocyte count and the polymorphonuclear count.

The Position of the Urinary Bladder During the Latter Months of Pregnancy and Labor.—PARAMORE (*Jour. Obst. Gyn. Brit. Empire*, March, 1909) reviews the literature of this subject, and describes dissections of his own to determine the position of the urinary bladder during the latter months of pregnancy and labor. He concludes that during the latter months of pregnancy the bladder is already in part an abdominal organ, and that its transplantation is completed before the actual mechanism of delivery of the fœtus is commenced. The bladder does not form a part of the pelvic floor in any way. As the child descends the other pelvic contents rise until the fœtus comes upon the actual pelvic floor. For birth to occur the fœtus must pass through the muscular tissues of the pelvis, and thus with the coccyx and anococcygeal ligament, support the pelvic viscera, preserve the intra-abdominal pressure, and perform the functions of the pelvic floor in securing rotation.

GYNECOLOGY.

UNDER THE CHARGE OF

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Atresia of the Vagina with Hematometra, Hematosalpinx, and Hematovarium.—A. BROTHERS (*Post-Graduate*, twenty-fifth anniversary volume, New York, 1908), taking a case as a basis, has prepared an elaborate paper on gynatresiæ, emphasizing the etiology and surgical treatment of the various modifications. He classifies the gynatresiæ as follows: (1) Primary blood-retention: from (*a*) malformations of Müller's ducts; (*b*) from adhesions acquired in embryonal or early infantile life. (2) Secondary blood-retention; (*A*) non-puerperal, (*a*) from traumatism (operations, neglected pessaries, injuries, etc.); (*b*) infections (scarlatina, smallpox, diphtheria, etc.); (*c*) natural (old age, atrophy, chronic catarrhal inflammations); (*d*) mechanical

(ball-valve tumors in the uterus, pressure of tumors at uterine cornua on tubes, uterine flexions, carcinoma, etc.); (*B*) puerperal inflammations with ulceration or gangrenous destruction of the cervical or vaginal mucosa. Fuld, in 1888, collected 65 cases of gynatresia with hematosalpinx, in which there was a mortality rate of 74 per cent. Of the 48 fatal cases, 9 died without operation. In 27 of the fatal operations the hematosalpinx occurred in a single genital canal. In the remaining 12 fatal cases the utero-vaginal canal was double. From 1888 to 1908 Brothers found recorded 164 cases of blood-retention associated with gynatresia, as follows: (1) Primary blood-retentions: (*a*) single genital canal, 80 cases; (*b*) double genital canal, 65 cases. (2) Secondary blood-retentions, 19 cases. In none of these did Brothers find a spontaneous rupture of a hematosalpinx with fatal peritonitis. Fuld found 3 cases of spontaneous rupture or evacuation of primary retention tumors with a successful outcome. It occurred through the obliterated area, or into the bladder or rectum or through the septum of a double uterus. Brothers found 7 others.

Uterine Fibromas Complicating Pregnancy.—GILLETTE (*Amer. Jour. Obst.*, 1908, lviii, 870) states that even very small fibroids of the uterus complicating pregnancy may be so situated as to become of lethal significance; that fibroid tumors of the uterus may disappear during or shortly subsequent to pregnancy; that not only pedunculated uterine fibromas, but interstitial ones as well, may be removed during pregnancy without interrupting the gestation; and that such operations should not be limited to the first half of pregnancy.

The Care of Patients after Abdominal Section, with Special Reference to the Period of Time They Should be Kept Recumbent.—FREDERICK (*Jour. Amer. Med. Assoc.*, 1908, li, 834) believes the wounds of abdominal section should be closed by absorbable suture material placed in tiers, and that the patient should be kept in bed from sixteen to twenty-one days. Reference is made to the absence of firm union in such wounds until two weeks have elapsed, to the exhausted state commonly noted as a result of the disease indicating the section being made, and to the advantage of prolonged rest in such condition.

Arteriosclerosis of the Uterus.—C. M. REES (*Amer. Jour. Obst.*, 1908, lviii, 748) states that a diagnosis of arteriosclerosis of the uterus is difficult to make, and can only be made when it is possible to exclude every other cause of hemorrhage from the uterus, and by microscopic examination of scrapings from the uterus, in which sclerosed capillaries are found, or, finally, from sections of such a uterus after its removal. Rees believes arteriosclerosis, as a definite cause of hemorrhage from the uterus, occurring in women between the ages of forty and fifty and among those who have borne children, is of greater importance than has generally been determined, and that in a fair proportion of cases the hemorrhages from the uterus are in themselves sufficient to endanger the life of a woman, and can be made to yield only to hysterectomy. Rees states further that, with the uncertainty of diagnosis even after examinations of a section from the cervix and scrapings from the uterus,

which show no evidence of malignancy, in women between the ages of forty and fifty who have borne children, and suffer with frequently recurring hemorrhages, hysterectomy is justified.

Cystocele.—I. S. STONE (*Amer. Jour. Obst.*, 1908, lviii, 953), after referring to the literature of the surgical treatment of cystocele, mentioning the material technical improvements contributed by Sanger, Hadra, Schauta, Wertheim, Watkins, Reynolds, Noble, Goffe, and others, gives details of the technique of the procedure he had independently evolved ten years or more ago. Free separation of the bladder from the cervix and vagina is the essential feature of the plan.

Genital Tuberculosis.—AUGUST MARTIN (*Jour. Amer. Med. Assoc.*, 1908, li, 968) advocates a careful search for bacilli in every case of genital tuberculosis and to depend absolutely upon the bacteriological diagnosis in order accurately to study the subject. Martin is convinced that 24.6 per cent. of the seriously diseased adnexa of patients in his clinic at Griefswald contained tubercle bacilli. The presence of clinical tests and even of tubercles was discarded as positive evidence of tuberculosis. The subconjunctival instillation of Pirquet-Calmette is regarded with much favor by Martin, who believes it is of special value in genital tuberculosis complicated by pregnancy.

OTOLOGY.

UNDER THE CHARGE OF

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The Pathological Anatomy of the Ear in Hereditary Syphilis.—ASAÏ (Kiobo), Wiesbaden, 1908. The material forming the basis of the author's brochure consisted in 20 fœtal and two-months-old temporal bones. In the middle ear there was found merely vessel dilatation and cellular infiltration, with the exception of 6 cases in which there was evidence of an inflammatory process, a percentage not evidence of preponderance in luetic cases. In the labyrinth the nerve distributions were normal with the exception of one case, in which, presumably as the sequence of a fœtal meningitis, there was cellular infiltration and connective tissue cells determinable between the ganglion cells; hemorrhage was determined in 7 of the petrous bones, but there was no evidence of luetic changes in the vessel walls. In 25 per cent. the observed defective development of the petrous bone corresponded to the period of gestation, and, as a whole, the results obtained from the investigation were negative, a conclusion in accord with the clinical observations in hereditary syphilis that the aural manifestations of this disease are comparatively rare, and are mostly evidenced at the end of the first decade.

The Hyperemic Method of Bier in Otology.—THEODORE HEIMAN (*Ann. des mal. de l'or., etc.*, January, 1909) states that Bier, in his book on hyperemia as a remedial measure, published in 1907, reports 17 cases of acute mastoiditis, of which number 16 were completely cured by this method, the hearing becoming, eventually, practically normal, with one exception; opening of the mastoid process was indicated in all of the cases, and the minimum duration of the hyperemic treatment was three weeks. In the chronic cases there were two complete recoveries. In Heiman's paper, after a comprehensive review of the literature of the subject, including quotations from Bier, from Fröse, who regards the anatomical conditions as unfavorable, and from Isemer, who found, in the cases in which it was ultimately necessary to operate, an unusually extensive bony necrosis, the author reports 8 cases under his own observation, and draws the following conclusions: (1) The clinical observations upon the effects of hyperemia are as yet insufficient to afford definite conclusions as to its value in diseases of the ear. (2) In the application of hyperemia in recent, and moderate, acute inflammations of the middle ear, coincidently with a paracentesis of the drumhead, it is possible to retard and ameliorate the disease. (3) Hyperemia facilitates the diagnosis of the latent purulent centres in the mastoid and in the temporal bone; it is contra-indicated in the more serious cases and in those in which there is any indication of intracranial complication. (4) The dissipation of the intracranial symptoms, which follows the hyperemia, is not to be regarded in favor of its use, but rather as a disadvantage, from the point of view of diagnosis.

The Treatment of Acute Middle Ear Suppuration with Nipple-shaped Perforation, by Aspirating the Pus into the External Meatus.—O. MUCK (*Archives of Otology*, December, 1908) states that in 150 cases of acute middle ear suppuration he found 5 cases, in the subacute stage, with a pronounced cone-shaped enlargement surrounding the perforation in the posterior superior segment of the drumhead. In these 5 cases, varying from one to thirty years of age, with previous symptoms of recurrent pus retention, recovery was effected, in an average of eight days, under treatment by repeated application of suction through the external canal, the duration of each application and its frequency being limited by the appearance of sanguinolent discoloration of the aspired secretion. The causative condition of these nipple-shaped projections Muck refers rather to the loose connective tissue network between the incus, stapes, and the medial wall of the tympanum, toward the antrum, than to the general swelling of the tympanic mucosa. He advocates treatment by aspiration rather than by incision of the nipple or by counter-opening, as recommended by Schwartz, on the ground that repeated aspiration affords a more adequate relief, favors the corrective hyperemia of the swollen tissues, and minimizes the liability to narrowing of the nipple sinus by epidermal involution. This method of treatment is inapplicable in cases in which involvement of the mastoid is evidenced.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF
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The Purification of Drinking Water with Ozone.—ERLWEIN (*Bericht über den XIV Internationalen Kongress. f. Hyg. und Demog.*, 1908, iii, 195) enters quite fully into a discussion of this subject. The first attempt to sterilize water with ozone was made in 1889 with an apparatus manufactured by Siemens and Halske in Berlin, and was reported by Fröhlich; although this experiment was quite a success, the method was not pushed. In 1893 the ozonization of water was taken up by the late Baron Tindal, of Holland, and exhibits of the machinery were made at Brussels and Paris in 1895, and again in 1897. A bacteriological study of the water purified by Tindal's apparatus was made by van Ermengem. Since Tindal's death his method has been modified and developed by Frise. Other modifications of this method of purifying drinking water have been made by Abraham and Marmier and Otto in France, and by Vosmaer in Holland, while in 1898 the Simens and Halske apparatus in Berlin was again put into operation. Erlwein presents a valuable chronological development of the ozonization of drinking water, but his special report is devoted to the study of the process as carried out at Wiesbaden and Paderborn. In these places the apparatus is that of Siemens and Halske. The plant at Wiesbaden is only contributory to a larger supply, and furnishes 250 cubic meters of water per hour, but it is not run continuously. The water from the plant has been carefully studied both chemically and bacteriologically at the Fresenius laboratory, and the results have been found to be satisfactory when the apparatus is not overworked. The Paderborn plant has been in operation for five years, and supplies from 80 to 90 cubic meters per hour. The water supply of this village is at certain times of the year quite satisfactory, but it is quickly and greatly polluted by rains; and two typhoid epidemics, one in 1895 and the other in 1898, caused the authorities to seek some method of purification. The plant was installed in 1902, and there has been no typhoid fever since, at least no epidemics. The ozonized water taken at a distance of 50 meters from the ozonizing tower gives no ozone reaction, has no unpleasant odor or taste, and does not corrode the water pipes. The cost of the process is 2.5 pfennigs per cubic meter, but Erlwein states that with a larger plant this might be reduced to 1 or 0.5 pfennig. Costly repair has not been necessary. The number of bacteria per cubic centimeter in the raw water varies from 100 to 5000, and that in the ozonized water from 0 to 22.

At the same Congress, Courmont and Lacomme (*Ibid.*, 215) report on this method of water purification as practised in France. In this country the methods are three, that of Frise, Otto, and Abraham, and Marmier. The first is in operation at Saint Maur, in Paris. The water is that of the Marne, and this is clarified by coarse filtration before

being ozonized. It requires 35 kilowatts per 1000 cubic meters. Two grams of ozone per cubic meter of air, and 30 c.m. of air to 40 c.m. of water are used. This is equivalent to 0.6 gram of ozone per 1000 c.c. of water. The discharge is 108 c.m. per hour. The cost is 0.015 francs per cubicmeter. The result is excellent physically, chemically, and bacteriologically. The ozonized water is clear, of good taste, without odor, and shows no appreciable chemical alteration, no nitrite, and no increase in nitrate. Before filtration the number of bacteria was found to be 4000 with many coli; after, it was 7 with no coli, showing a reduction of 99.8 per cent. The Otto system has been in operation at Nice since 1903. The requirement is 0.5 gram of ozone per cubicmeter of water. The chemical composition is not modified except that the organic matter is reduced. The number of bacteria is reduced per cubic centimeter from 2000 to 1.4, with total disappearance of coli. The cost is 0.005 francs per cubicmeter, this very low cost being due to the fact that the electricity is generated by water power. The process of Abraham and Marmier is in operation at Lille. The quantity of ozone used amounts to from 4 to 6 grams per cubicmeter. A commission, of which Calmette and E. Roux were members, investigated this process and reported that it is quite satisfactory. The raw water contained 1517 bacteria per cubic centimeter, and the ozonized 0.03, Bacillus subtillis being the only organism that escaped. The same method is in operation at Cosne-sur-Loire, and is satisfactory there also.

[It seems evident from the above that the purification of drinking water for municipalities by ozonization is of much promise. The methods will doubtlessly be improved from time to time. Its applicability to waters containing much organic matter in addition to the living organisms, is a matter that will need more extended study. When this matter is in suspension it can be easily removed by coarse filtration, but when in solution one would expect that ozonization in order to be efficient would be much more costly than the above given figures indicate.—V. C. V.]

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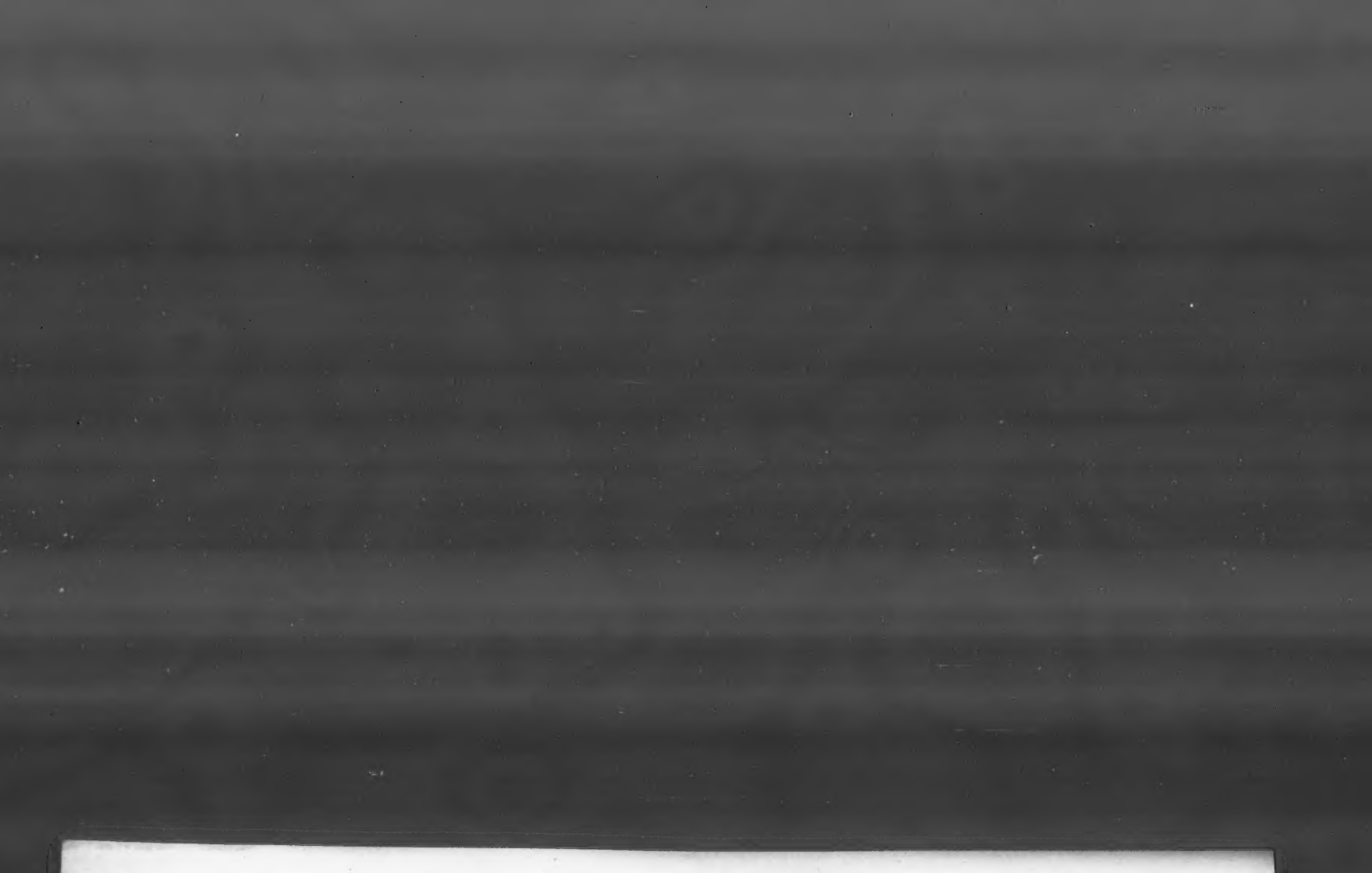

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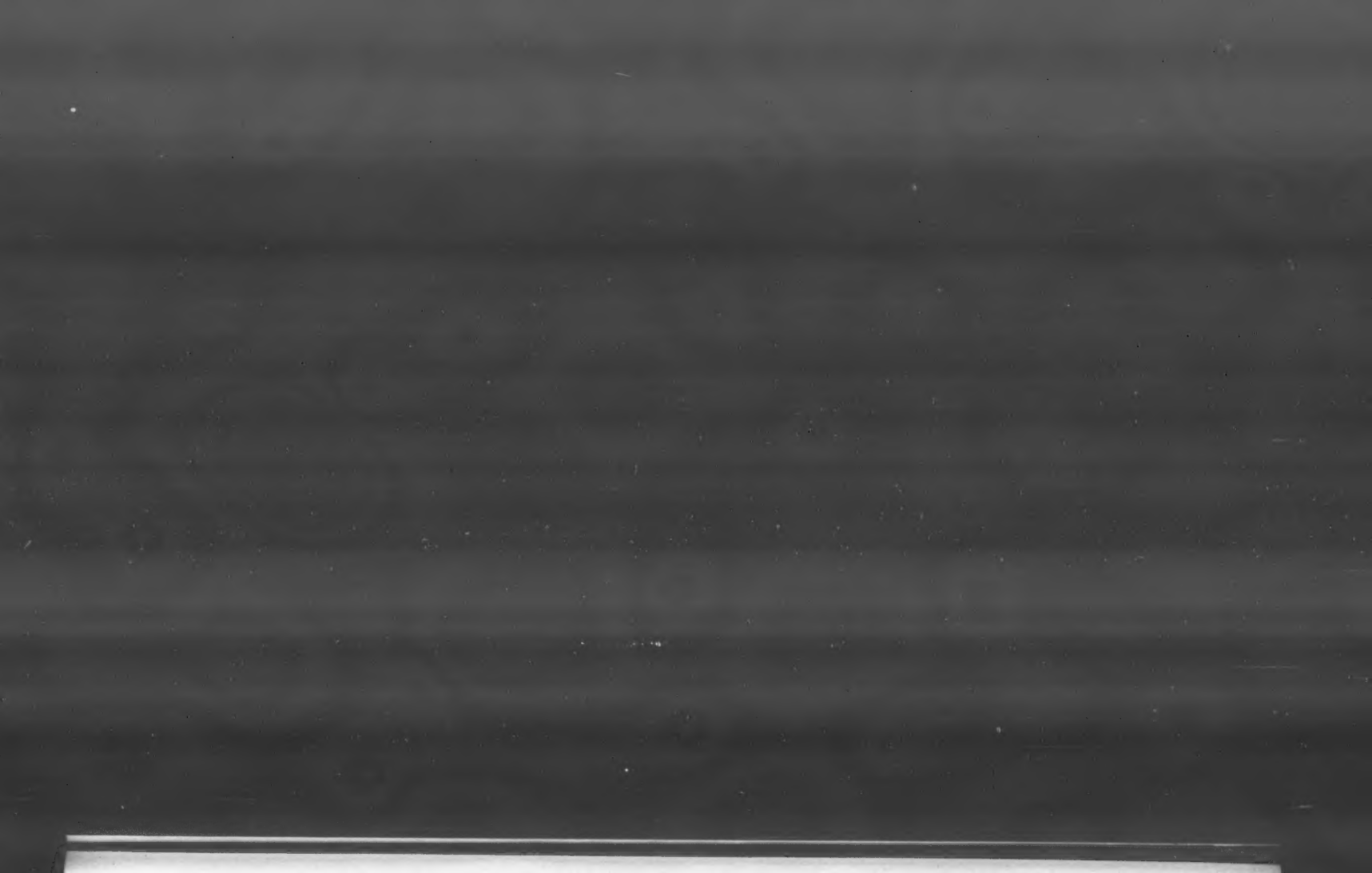

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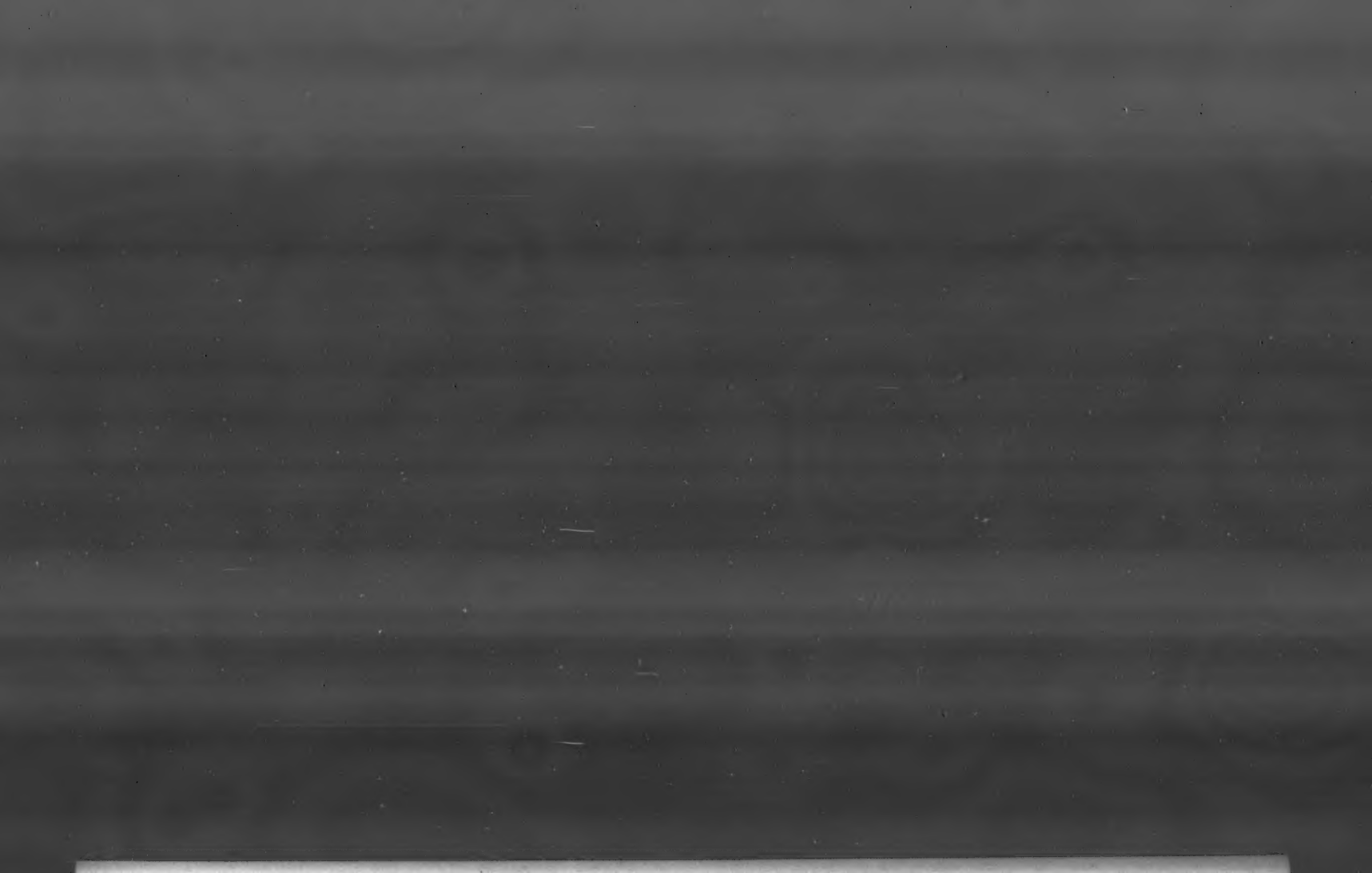

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